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ENDOCRINOLOGY NUMBER—DR. MAXIMILIAN KERN, COLLABORATING

Medical Lib.

# CLINICAL MEDICINE and SURGERY

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Vol. 35, No. 7

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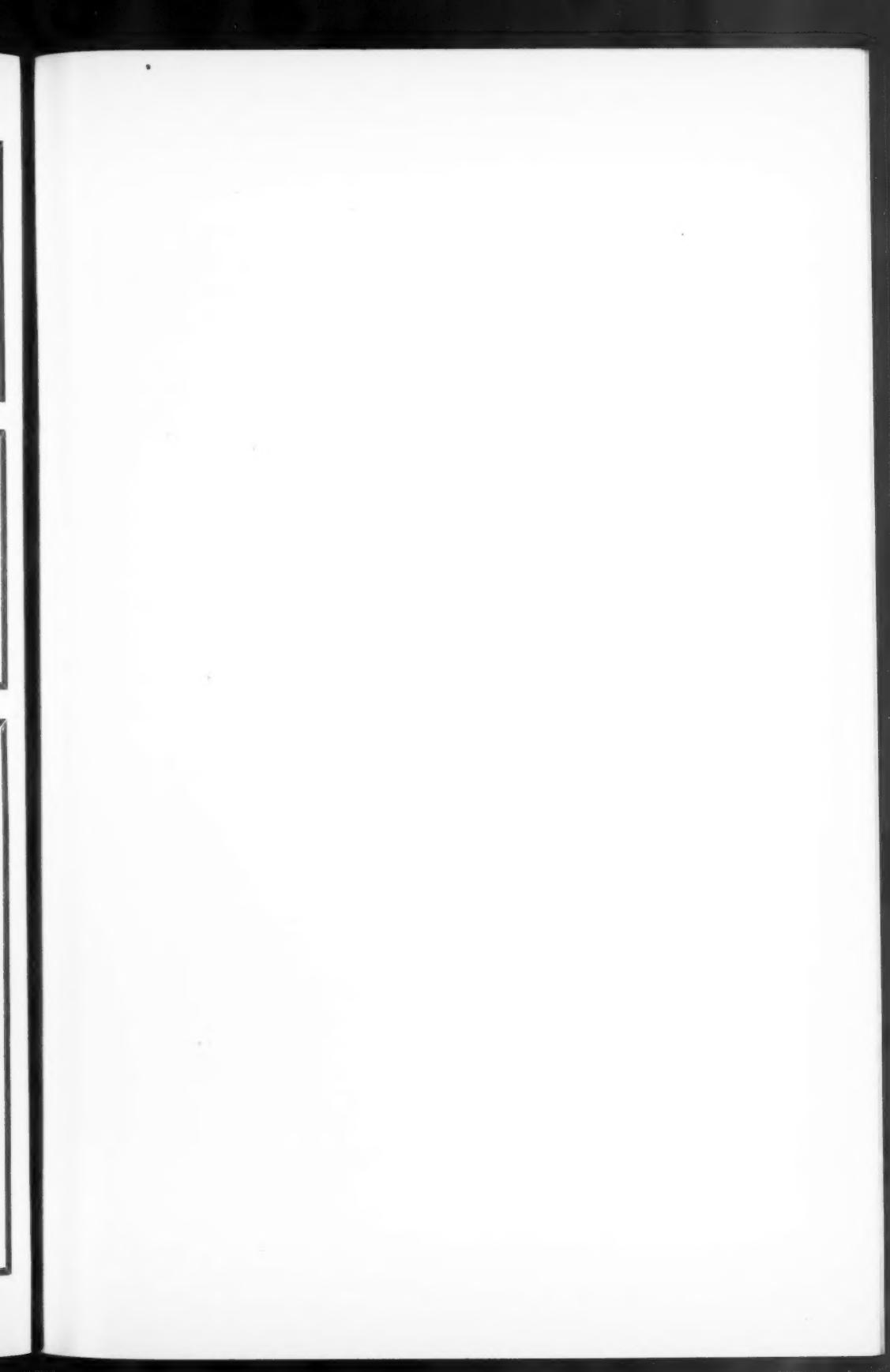
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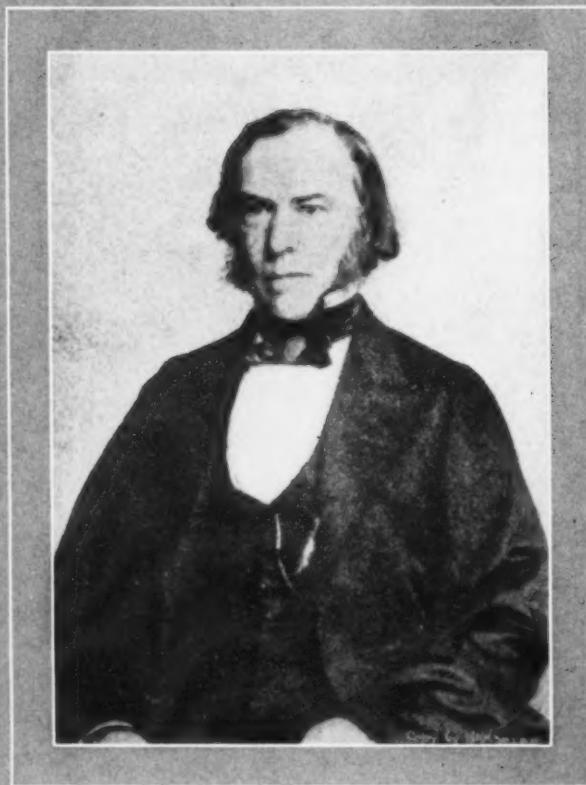
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CHARLES EDWARD BROWN-SÉQUARD, M.D.



# Clinical Medicine and Surgery

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## Dr. Charles Edward Brown-Séquard

IT is sometimes difficult for us to remember how young, as a science, medicine is, when we remember how immemorially old it is as an art. Less than three-quarters of a century ago, the ductless glands were an unexplored territory. Some of the hardy pioneers had glimpsed several of the mountain peaks of that fascinating region, but most of the writings on the subject consisted of flights of the imagination, many of which have, however, been translated recently into reasonably solid, scientific facts.

Among the earliest and the boldest explorers of this field was Charles Edward (or Édouard) Brown-Séquard, an enthusiastic and active soul who made his mark as a scientist and investigator.

He was born in Port Louis, on the little island of Mauritius, a British possession in the Indian Ocean, about 600 miles east of Madagascar and in a south latitude corresponding to that of Mexico City and Bombay, India, to the north. Though his father was an American—a native of Philadelphia—and his mother a French woman, he always considered himself a British subject; but the warm, Celtic blood inherited from his mother showed itself throughout his eager, restless and versatile career.

He pursued his professional studies in Paris, and after his graduation in medicine,

in 1846, he returned to his native island, intending to practice there; but the field was too limited for his developing talents and roving disposition, so, in 1852, he came to the United States, stayed a few years, and then went back to Paris, where he engaged in some of his important researches.

It was during this Paris period, in 1856—one year after Addison had published his monumental treatise on disease of the suprarenal glands—that Brown-Séquard succeeded in producing, in various animals, exaggerated symptoms of Addison's disease, by removing the suprarenal capsules; and also demonstrated the further important fact that, if the blood of normal animals was transfused into those which had lost their adrenals, these latter could be kept alive for some time after they would, under the circumstances, have died, thus proving that the suprarenal glands secrete a substance necessary to life.

His endocrine researches were, however, at this time, somewhat in the line of a side-issue to his principal work in physiology, and especially neurology. Though his name is usually associated, in the minds of most people, with his studies of the ductless glands, it must be remembered that his

contributions to neurology were numerous and of great importance. It was he who first demonstrated the decussation of the sensory fibers in the spinal cord, among other things.

His stay in Paris, on this occasion, was not long. In 1859 he went to London, where he became physician to the National Hospital for the Paralyzed and Epileptic, in which position he remained for five years, expounding his interesting views on the physiology and pathology of the nervous system.

In 1864 Brown-Séquard crossed the Atlantic for the second time, and became professor of physiology and neuro-pathology at Harvard University. Here he stayed for four years, until his French blood and his fame recalled him to Paris, in 1868, and to the professorship of pathology in the *École de Médecine*.

But the conflict of strains within him—British birth, of French and American parentage—again set him traveling west. In 1873 he again returned to America, where he engaged in medical practice in New York City, until, in 1878, he was, once more, recalled to Paris, to succeed Claude Bernard as professor of experimental medicine in the *Collège de France*. His blood seems to have cooled somewhat (he was then 61 years old), for he settled down in this position and retained his chair until his death, which occurred April 2, 1894.

Among the experiments most frequently associated with Brown-Séquard's name were those he made in 1889, at the age of seventy-two, by injecting testicular extracts into his own body, by which he felt himself greatly reenforced in general, muscular and mental power and activity. These injections were subjected to ridicule by many of his contemporaries, the 1910 edition of the ultra-conservative "Encyclopedia Britannica" speaking of them as an unfortunate foible of senescence. Even today, in the face of the extensive and careful work along this line which has been reported, there are those who, like the writer in the famous book of reference just quoted, have seen no new light on this subject in the last forty years.

Brown-Séquard was a keen and accurate observer and a confirmed and enthusiastic experimentalist throughout his life, and his researches have been published in about 500 essays and papers, chiefly in the *Archives de Physiologie*, of which he was one of the founders.

To his brilliant intellect and tireless energy we owe much of the painstaking, fundamental labor and study which seem now in a fair way to place endocrinology among the valid and respectable sciences.

Endocrinology is still in its embryonic stage, but some day it will be revealed as the most important of all medical sciences.—Manly P. Hall.

#### THE "PERSONALITY GLANDS"

Human personality is the sum of all the physical factors—height, weight, body conformation, the texture and pigmentation of the skin and hair, muscular development, and various other matters—which permit one man or woman to be distinguished from all other human beings, plus those emotional and mental reactions to the circumstances and vicissitudes of life which constitute the general psychic coloring, which differs somewhat in every individual.

Some of these physical personality traits are conferred upon us by the germ-plasm of our parents and are difficult or impossible to modify by any voluntary physical or mental efforts of ours: Others develop later in life and are the result of physical and chemical changes in the body, over which we have more or less direct and positive control.

All physical changes, of whatever nature, are brought about by means of some physical mechanism. That this general law applies to changes in human personality is only beginning to be recognized. The most thoughtful students of these problems are coming to believe that the mechanism of those recondite alterations in physical appearance and behavior, with which most people are more or less familiar, resides in the endocrine glands.

One might say, off hand, that a dark skin is the racial heritage of certain peoples. It is true enough that, so far as we know, no endocrine disorder can make a Chinaman or an Ethiopian out of a white man. But a case of Addison's disease can make the patient's skin darker than that of many negroes; and an attack of jaundice (which may have more endocrine factors than we now realize) may give the patient a color which any Mongolian might envy.

The coloring of the iris is probably a strictly mendelian characteristic, and the color of the hair may be largely of that nature; but what other personal characteristics are there which cannot be altered by changes in the endocrine organs—unless,

perhaps, it be the innate degree of susceptibility of these organs themselves to stimulation or damage by external forces?

The height? No. That can be increased, even to gigantic proportions, by an overactive pituitary, or stunted to dwarfism by a lack of activity of this and other glands.

The weight? Obviously not! That becomes increased when the gonads and pituitary fail to function, and reduced to emaciation in some cases of exophthalmic goiter.

The abundance and distribution of the hair suit and the texture of the skin? Oh, no! The amount and location of the hair on the body is determined to a considerable degree by the adrenals and to some extent by the pituitary and the gonads. The skin of a patient with Addison's disease is brown and leathery; that of one with myxedema is thick, pale and filled with a mucoid exudate. Even the nails and teeth are affected by endocrine disorders.

The contour and expression of the face? Hardly! In acromegaly, myxedema and advanced cases of Graves' disease the expression, and even the shape of the face are changed beyond recognition within a few years. The dull and idiotic countenance of a cretin or a mongolian idiot can be so altered, in a few months, by properly applied organotherapy, that even the parents would scarcely know their own child.

Do inalienable personal characteristics then reside only in the psychic reactions of the individual?

Not even here. The lively, sparkling, vivacious person, popular in all social gatherings, may, and frequently does, possess those traits because of an overactive thyroid; while those who are considered gloomy, grouchy or lazy may deserve those unpleasant judgments solely by reason of deficiencies in thyroxin or in the secretions of the pituitary, gonads or suprarenal capsules or any combination of these and other glands.

Even the outstanding features of maleness or femaleness, which are such important factors in what we call personality, are determined by the activities of the gonads. If these glands are removed in early life, the female child does not become a woman nor the male infant a man. And when they gradually cease to function, as old age comes on, the outstanding characteristics which distinguished the two sexes in their prime, melt away, *pari passu* with the advancing years, and both tend to revert, physically, to a common neuter type.

When we realize how intimately the autonomic nervous system, which initiates and conditions all our innumerable unconscious activities, is bound up with the endocrines, we begin to gain some idea of the profound and enormously potent effects, upon our lives and fortunes, which may be exerted by these small but prodigiously important organs.

There be those—the worshippers of the "old gods" in science and in medicine—who laugh at the enthusiasm of the students of the ductless glands and belittle their work because, forsooth, their results can not be duplicated in the laboratory. Not yet can the human body be seen through like a glass test tube; nor can the reactions of a sick man be accurately compared with those of a healthy dog or rabbit; neither have we been able to duplicate in any laboratory animal the physical effects of ambition, exalted love, worry or various other emotions which men and women experience and to which they react, each in his own way.

It would seem that, with the advances in our knowledge of the powers and functions of the ductless glands, we are gradually opening a door upon vistas of which we hesitate even to dream. It may well be that the future of endocrinology carries upon its shoulders the future progress of humanity to unimagined heights of attainment. Nor does it appear an exaggeration to say that, at the present day, no field of research offers such tremendous possibilities for remoulding the world's scheme of things, "nearer to the heart's desire".

Nothing was ever so unfamiliar and startling to a man as his own thoughts.—Henry D. Thoreau.

#### IS EXOPHTHALMIC GOITER A MEDICAL OR SURGICAL DISEASE?

The rich array of contributions to questions of live interest in endocrinology which fill the pages of the present issue of CLINICAL MEDICINE AND SURGERY call for little comment. These contributions are written by men of authority on the subjects treated; they are informative, and not intended to be revolutionary in nature. Their conservatism lends more importance and worth to their message. Endocrinology has made rapid strides since the days of Brown-Séquard and this progress is well reflected in this issue.

Bram's paper regarding the non-surgical treatment of exophthalmic goiter is so outstanding and of such vital interest that it

doubtless will attract a great deal of attention, as well as disagreement.

That the hyperthyroidism usually accompanying this disease is not a thyroid disease, *per se*, and is not a condition to be dealt with by destructive surgery is a matter which the writer has long advocated. The balance of evidence would appear to imply that this hyperthyroidism is compensatory—forced upon the thyroid, which must either deal with the increased systemic toxemia, or suprarenal dysfunctioning will follow.

There is little or no agreement regarding the many theories of exophthalmic goiter. One need not dwell on these various theories but merely say that we probably must look to Moebius for the view that exophthalmic goiter is a purely thyroid condition. However, from the many conflicting views of today, one fact stands out rather clearly; namely, that so-called exophthalmic goiter may not be goiter at all, and that the hyperthyroidism which usually accompanies it is a concomitant defense action of the organism. Many cases of Graves' disease are met with, clinically, in which there is no hyperthyroidism, as expressed in terms of *basal metabolism*. On the other hand, the characteristic symptoms of Graves' disease may disappear under appropriate treatment, while a high basal metabolism persists.

Among those who disbelieve in the thyroid origin of exophthalmic goiter may be mentioned Cannon, Crile, McCarrison and Leonard Williams.

Although it seems rather premature to suggest the real basis of exophthalmic goiter, much may be said in favor of the view expressed by Hutton and others that the disease is really of suprarenal origin. Marine and Bauman have recently shown that destruction of the suprarenal cortex brings about symptoms similar to those of exophthalmic goiter. The views of Bram, that the condition is a constitutional one—a neuroendocrinopathy—are very convincing and will rouse serious attention.

In any case, it seems to be fairly clear that, in the face of the uncertainty as to the real origin of exophthalmic goiter, destruction of the thyroid gland, either by surgery or radiation, is neither a rational procedure nor is it indicated. The thyroid enlargement may be a necessary compensatory or defensive action on the part of the organism, and removal of the gland may be an injury rather than a help to the patient. Bram has clearly

shown the ill effects which may follow such surgery. On the other hand, his excellent results from medical treatment of exophthalmic goiter will command much attention.

The surgical treatment of Graves' disease, which was initiated by the brilliant performances of Kocher and De Quervain, has had its day and it may be well now to call a halt to this practice.

MAXIMILIAN KERN, M.D.

An ounce of inquiry is worth a ton of acquiescence.—Ernest Wood.

#### CUPID'S MATURITY

The conventional representation of the god of love is as an engaging infant, dressed in a quiverful of arrows and an irresistible smile and armed with a bow shaped like the upper lip of a lovely girl.

What could a child like this know about love—no matter what interpretation one puts upon that much-abused word? Certainly nothing of sex love, for a young child is without sex. Still less of the tremendous emotional experiences which drive men and women on to almost superhuman achievements, or that deep and sublime union of minds which sometimes (but too rarely) binds a man and a woman together through a long lifetime of beautiful and fruitful mutual endeavor.

It is time that Cupid grew up! This looking at love with the eyes and the mind of a chubby baby is a frequent source of misunderstanding, sorrow or even disaster.

Time was, perhaps, when human attachments could blossom like a flower, harming no one by their consummation and breathing an exquisite fragrance; but those halcyon days, if they ever existed, are no more. The love affairs of primitive peoples, today, impress our sophisticated consciousness as rather coarse and brutish proceedings—however, they may appeal to the participants.

The days of "love in a cottage," subsisting on a diet of "bread and cheese and kisses," are a dream of the past. Love, to the modern member of our semi- or pseudo-civilized communities is a very complicated business, requiring a trained eye, a thinking mind and a reasonably mature judgment for its successful and permanent realization—such faculties as could never be the possessions of the round and rosy Cupid of the days of gorgeous valentines with borders of paper lace.

If we will consent to let that dear and anachronistic child come to a reasonable degree of maturity, we will go far toward solving some of our most pressing social problems. Let us picture him as a sturdy, clean-limbed, clear-eyed youth or maiden, not supersophisticated and *blasé*, but honest and reasonably intelligent—willing and prepared to know the truth and to cope with the facts of modern life.

So long as young men and women follow the specious glitter of attraction with the eager and unreasoning enthusiasm of children; thus long will many of them find that the enticing road they follow ends in the bog of sorrow and disgrace, the thirsty and pitiless desert of frustration and disillusionment or the craggy and bone-strewn rocks of wreck and despair.

The child reaches for the object of its momentary desires without thought of the future, for it knows neither future nor past.

In the first glamor of the stirrings of sex it appears to the bemused one that union with this boy or this girl would be the supreme crown of life. This is natural and well. Without this cosmic urge our world would be a barren and joyless, burned-out star. But let the foresight of enlightened adolescence shine upon the road. This girl is an exquisite thing—now; but what does her mother look like? An evening in her society is a foretaste of heaven—now; but how about sitting opposite her at the table, three times a day, for fifty years? The propounding and straightforward answering of questions like these are functions of the maturer Cupid who must develop, if sanity is to rule the coming days.

So let the little Love grow up; welcome him in this newer manifestation and learn eagerly the beautiful and indispensable lessons which he has to teach us. So, and so alone, will men and women come into the glorious heritage of "Love, the beloved republic, which feeds upon freedom, and lives."

To love abundantly is to live abundantly, and to love forever is to live forever.—Henry Drummond.

#### ARE WE ALIVE?

One of the most prominent characteristics of a living organism is that it *grows*—in size, first, until it has attained the limit set by nature for its type or species, and then in quality.

A man grows *larger*, from the moment of his birth until he has attained full adulthood. From then on his growth consists in

enlarging, not his stature, but his powers and abilities; his knowledge, sympathy, wisdom and compassion; and this should continue as long as he lives. In fact, it actually *does* so, for, if the process of growing stops, the man is *dead*, even though his carcase may continue to wander about and go through the motions of living. Where there is no growth there is no true life.

The quality of *livingness* does not, however, come to us from some outside source. If it is present at all it is generated *within* us in some manner which has, so far, eluded the researches of Science. The *pabulum* for growth comes, to be sure, from our environment—the food which we eat, for growth in size and for compensating the wear and tear of daily activity; *experience* to nourish our faculties and powers and build up our wisdom and understanding.

But while our physical and psychic aliment comes from without, that property which enables us to build it into our permanent structures, to each part according to its need, is inherent in us, as living beings—God-given, if you please, but not as some benefaction conferred upon us from a remote source; rather, because there is something essentially godlike within us, in that, after our humble fashion, we are *creators* and arbiters of our own destiny.

Sometimes the life force within grows feeble, flickers or smolders. Then we must, by some means, stir it up and fan it into a blaze. The fuel for this divine fire is all about us, if we will but step forth and gather it; but it will never, of itself, come in and cast itself upon our pale and smoky hearth.

A couple of millennia ago the promise was made to mankind, "Seek, and ye shall find!" The "finding" is not accidental, and it is not for loafers—only for "seekers." Neither does it mean the finding of *things*, primarily, but of strength and abilities. Howbeit, the same Teacher said, "Seek righteousness (which means merely the *right way* of doing *right deeds*) first, and all *things* shall be added." Perchance He meant what He said. It is worth trying.

A dead fish can float with the stream. Dead wood can remain in the same condition for centuries. It takes a live trout to swim up the river and a living tree to grow.

Growth is the measure of life. If we can find out how fast we are growing, we can judge how fully we are living—or whether we are truly alive at all.

### ENDOCRINOPATHIES AND FOREIGN PROTEINS

The part played by foreign proteins in the causation and treatment of disease has occupied a good deal of space in the periodical medical literature for several years, but we still appear to be working along this line more or less empirically and have probably only scratched the surface of the subject.

The condition we call allergy is apparently closely associated with the presence in the body of certain protein substances which are abnormal to it. These may have been injected parenterally, as horse serum; ingested orally, as certain types of food to which certain persons are sensitive; or deposited on the mucous membranes, as in the case of hay-fever.

But how much of the allergic syndrome is actually due to these extraneous substances? And how much to some little-understood perversions of body chemistry which may predispose the patient to hypersensitivity?

Most people can eat, without distress, eggs, cheese, strawberries, oysters and the other foods which have an evil reputation as inciters of allergic manifestations. Most patients can be given, without danger, an injection of diphtheria or scarlatina antitoxin. Only a relatively small proportion of the population suffers inconvenience during the season when the ragweeds and other "hay-fever plants" are pollinating. Why?

There seem to be reasonably adequate grounds for believing that these individual conditions of hypersensitivity to substances which, for the majority of people, are innocuous, may rest upon certain insufficiencies in the structure or functions of some of the organs of the body. This position is fortified by the work of Adam, Haseltine, La Forge and others, in connection with asthma, by which this disease, long classified in the allergic group, as well as other manifestations of hypersensitivity, has been relieved or cured, chiefly by clearing out waste products (which may

contain abnormal proteins) and by normalizing the body chemistry.

It is well known that some of the skin symptoms of the allergic state—such, for instance, as dermatographism—are frequently present in patients suffering from thyrotoxicosis; and in this issue (p. 487) Novak has rather convincingly connected hyperesthetic rhinitis (another condition believed by many to be allergic) with deficiency of thyroid secretion.

The parenteral administration of certain foreign proteins—boiled milk, peptone solutions, serums, vaccines, etc.—is now being widely employed in the treatment of many types of infections and may prove to be of value in all infective diseases. These measures cause an increase in the number and activity of the leukocytes, but what other changes they may cause in the tissues and fluids of the body is still, more or less, a mystery.

In Stanley's article, on page 506, the results of the parenteral injection of liver substance are shown; but, in the case where testicular substance was implanted, the effects were strikingly similar. May not all the phenomena observed have been due to the body's reaction to the foreign protein, rather than to any specific action of the material used?

It seems, also, entirely possible that the changes in blood pressure produced by autocondensation and other physical agents may depend upon the release of certain secretions which act to neutralize deleterious substances present in the body, and that the alterations in metabolism which follow otophoresis may rest upon a similar basis.

This whole question of foreign proteins and their behavior in the human organism is one of deep interest and serious importance, and it is to be hoped that the research workers will devote much attention to its solution in the years immediately following, and will be able to give us sound and demonstrable reasons for the clinical results which more or less regularly follow our rather fumbling employment of these substances as therapeutic agents.

# Leading Articles

## Minor Degrees of Endocrine Dysfunction

By IVO GEIKIE COBB, M.D., M.R.C.S., I.R.C.P., London, Eng.

THE recognition of early degrees of endocrine dysfunction is of great importance, and this for several reasons. First of all, for the obvious reason that the earlier any disease is recognized the quicker it is arrested; secondly, any advanced condition does not lend itself to treatment, from the curative point of view, to anything like the same extent, because the disorder, originally functional in nature, may well have been followed by organic and structural lesions. Again, we do not know how much of each hormone is secreted from any endocrine organ in a given time, and therefore, in advanced cases, it is at least possible that we are never able to supply adequate quantities to replace the normal secretion.

Life consists in the perfect action and interaction of the various endocrine organs; in fact, in their play upon the various systems of the body. The result is a sound mind in a sound body. Now, when one is beginning to suspect endocrine dysfunction in any individual, by far the soundest plan is briefly to run over the various endocrine organs to see whether there are any signs of deficiency or excess of one of the internal secretions.

### The Thyroid

Minor degrees of thyroid underaction are well recognized and usually easy to remedy. Minor degrees of thyroid overaction, while easy to recognize, are somewhat difficult to treat, because the thyroid is an organ which is called upon periodically, especially in the female sex—to some extent in both sexes—to put forth an increased endeavor. Just as it is sometimes undesirable to lower a temperature, so is it sometimes undesirable to interfere with a minor degree of thyroid over-function.

Its recognition, however, should be a simple matter. The increased rate of the heart beat, the height of basal metabolism, the tendency to fulness of the gland itself, the normal or supernormal temperature—these all point to a state of over-action of

the thyroid, which, however, may be only temporary.

Again, take the neighbors of the thyroid, the parathyroids. The signs of over- and under-action of these glands are now recognized, and although not so well established or capable of proof in the same way as is dysfunction of the thyroid, yet they are sufficiently plainforward to be recognized, and, what is even more important, to be capable of treatment.

### The Parathyroids

The parathyroids are intimately concerned with the metabolism of lime. In states of over-function there is a disturbance of calcium metabolism; there is a calcification of arteries, a rise of the blood pressure, calcium deposits in, and, possibly, fibroid degeneration of, some organs, among these being the kidneys and liver.

When we come to deal with under-function of the parathyroids we realize that we are on firmer ground; for removal of the parathyroids (without interference with the thyroid) has shown what results follow this operation in animals. There is, of course, the well recognized, postoperative tetany. There is decreased calcium in the blood; there is interference with bony growth; there are vasomotor disturbances, and the well known mental and nervous manifestations which are very often benefited by administration of extracts of these glands. Among the other signs which we recognize as depending upon hypo-parathyroidism are dermatographia, erythema, possibly angio-neurotic edema, increase of the tendon reflexes, defects of the enamel, and possibly lack of tone of the stomach, with gastro-intestinal disturbances.

Long before our knowledge of the parathyroids was as complete as it is today, attention had been drawn by many writers, notably Sir James Barr, of Liverpool, England, to the importance of the lime, and he has pointed out that there are various devices present for measuring whether the

lime was deficient in the circulation or not. I quote from an article reprinted from the *Post Graduate* for December, 1910, in which Barr says, "From repeated observation I have come to the conclusion that it is the fixed lime which is concerned in the viscosity and the coagulation of the blood, and with both these phenomena the free calcium ions which are revealed by Blair Bell's method have, directly, nothing to do." After discussing the viscosity of blood in the capillaries, he goes on to say that, so far as the lime salts are concerned, the contraction of the arterioles and the action of the heart, are due to the free calcium ions. He adds, "Of course the secretions of the infundibular portion of the pituitary body and the suprarenals also lead to such contraction of involuntary muscular fibre, but we are not at present concerned with their extent or deficiency in the circulation."

I give these quotations to show that, since the work of the parathyroids in their relation to calcium metabolism was first understood, a good deal has been done, by thoughtful investigators, in the way of discovering the part played by calcium in the blood. I can recommend anyone interested in this subject to refer to this article by Sir James Bar; for, although it was written 18 years ago, it contains a great deal of very practical information.

#### The Pituitary

Turning our attention now to the pituitary gland, the states of over-function and under-function of this organ are full of interest to the endocrinologist. Dealing with hyper-pituitarism first, we may consider the clinical signs of overaction without considering, at this stage, whether the anterior, the posterior lobe, or the pars intermedia is concerned.

Generally speaking, the over-action of the glands is shown by accelerated metabolism, bony overgrowth, enlargement of the extremities, and one or two interesting signs, which go to show that the pituitary, at some time or other in the individual life, has been over-active. Among these are, large ears, widely spaced incisor teeth, a large tongue, a tendency to waxy, smooth, pale, skin, heavy hair, beard and eyebrows.

Under-action of the pituitary is shown, as one might expect, by signs opposite to these. Where there is under-action, there is under-growth, leading to a condition of dwarfism, or something akin to it; delayed development, if the condition arises early in life; obesity, amenorrhea in the female,

sometimes polyuria, occasionally eye lesions; the skin is pale and soft, an opposite condition to that seen in hypothyroidism.

It will be apparent, therefore, that, so far as the pituitary is concerned, with the vast influence it exerts on growth, a glance at the individual will often tell one some of the history of his endocrine organs, from such signs as hair, skin and build. It is stated, moreover, that certain blood changes are associated with hyper-pituitarism, and these are associated with cardiac hypertrophy, due partly, no doubt, to the accelerated metabolism, and partly to the retention of phosphates and lime salts which is said to occur in this condition. Moreover, the part which the pituitary plays in the sexual life of the individual is now well known. It would appear that the pituitary, acting of course in consort with other of the endocrine organs, is of the first importance in determining a normal sexual life. Many cases of amenorrhea, for example, have their origin in pituitary dysfunction, and are remedied by suitable and adequate treatment.

#### The Adrenals

In dealing with the adrenal system, we can describe, although not with any degree of certainty, signs indicative of over-action and under-action. Addison's disease stands by itself as an organic exhaustion, or destruction, of the adrenal glands.

Over-action of the chromaffin system may show itself by signs, some of which are often associated, or have been in the past, with hyperthyroidism. Take, for instance, the eyes. The proptosis was regarded as a cardinal sign of hyperthyroidism. It is now recognized that this is associated with chromaffin irritability. Many people show this sign, in conjunction with others which indicate sympathetic irritability—the tendency to perspire easily, the moist skin, the brilliant eyes, the copious and healthy looking hair, which are all signs of an adequate or over-active state of the chromaffin system.

What are the signs of underaction of this important system? It is difficult to answer this question with any degree of certainty, for other glands may be responsible for some of the signs which have often been described as indicative of hypo-adrenia. Among these are symptoms of deficient autonomic innervation, arterial hypotension, perhaps a weak myocardium, certainly muscular asthenia; and among the signs for which one can look is pigmentation of the skin, more particularly in parts which are

usually moist, like the axilla and the groin, on the chest and parts of the back, as well as the white line described by Sargent, which occurs on stroking the skin of the abdomen lightly.

#### The Sex Glands

Over-function and under-function of the sex glands, in both sexes, are capable of recognition. The state of overaction of these glands, *occurring before puberty*, tends to rapid growth, early closure of the epiphyses, *pubertas praecox*, early development of the menses and other changes which possibly are concerned with others of the endocrine organs. A state of over-function of the sex glands, *occurring after puberty* must lead to a modified picture, possibly characterized by excessive sexuality.

The state of under-function of the sex glands must vary in its clinical signs. It is suggested that, in the female, it leads to obesity and premature menopause. There are, of course, vasomotor disturbances and anxiety symptoms. In the male, the condition seen is a modified form of the characteristics of eunuchoidism.

But again, if the under-function occurs before puberty or after, the picture will vary accordingly. There have been different types described among recognized eunuchs; a tall thin type, and a large fat type. I think, personally, it is almost impossible to describe accurately a type which can be recognized as solely due to sexual dysfunction. Tumors of the adrenal cortex, leading to virilism in the female, and unduly early puberty in the male, pineal tumors, and other endocrine abnormalities, complicate the accurate diagnosis.

#### The Thymus

When we turn to the thymus, we have some very interesting hypotheses but very few definite facts. We know that enlargement of the thymus will lead to local symptoms, such as stridor and asthma, and to changes in the sex configuration. There have been changes described in connection with the sexual organs which are somehow referred to the thymus; and it is suggested that possibly the thymus may be concerned in undescended testicle. Certain it is that enlargement of the thymus is by no means so uncommon as is often believed. It is believed that an enlargement of the thymus, carried on into adult years, leads to dislocation of the metabolism of the body, such as is shown by fat, waxy flesh, pale skin, hairless face in males, and various cardio-vascu-

lar changes not difficult of recognition; but, in spite of these signs, it is exceedingly difficult, in many cases, to indict the thymus as the sole villain in the piece, but rather as one of the villains, or even, in some cases, as being more sinned against than sinning.

#### Endocrine Personalities

We have, of course, to know roughly the personalities which represent the dominance of one particular endocrine system. Recently there have been described pituitary personalities, as well as thyroid, thymus, sex gland, and adrenal-centered types. Every individual shows, to some extent, the particular stamp of the personality, and this depends upon the dominance of one endocrine organ and its secretion.

Now we must admit, straight away, that these are based upon a small amount of data and a large quantity of inference. That they will be capable of proof to a much greater extent than is at present the case there can be little doubt.

These personalities have been charted, so to speak, by comparing them with the types of individual which are recognizable from gross disorders, if not actual disease, of one of the endocrine organs. For example, the pituitary personality—the personality dominated by the pituitary—may be said to have arisen from the change of structure which is met with in a disorder such as acromegaly. Pituitary deficiency, that is to say, a personality resembling a typical hypopituitary individual, is easy to describe.

The thyroid personality—an individual governed by an active thyroid—is also a type which so closely resembles the Graves' disease patient that it is easy to see how the descriptions, which were first fully given in Louis Berman's book, have arisen. Thyroid deficient—cretins, mongols, and like subjects—have in common certain characteristic features, and it is upon these features that a description of the individual personality dependent upon under-action of the thyroid is based.

A close study of the description of these personalities makes it very evident that there is a good deal to be said for the accuracy of the descriptions. For example, the pituitary personality, the thyroid personality, and, to a less extent, the adrenal personalities, are fairly definite in their delineation. There is always the objection that these types may vary according to several different factors; first, the age at which the particular over- or under-function commences; second, intercurrent conditions,

which affect others of the endocrine glands; third, the type to which the individual belongs by heredity.

It is very curious to note how, in some families, a particular type of personality is seen in most, if not all, of the members; it is also interesting to note the way one child will show the dominance of one particular endocrine gland, while a brother or a sister will follow another characteristic type.

The student of endocrinology will do well to bear in mind the description of the different endocrine personalities; for with these as a basis, it will help him to define the most important questions of all in diagnosis: Is it a case of early endocrine dysfunction, or are we simply dealing with an outstanding endocrine personality?

#### Endocrine Examination

As well as the characteristics of the endocrine personalities, there are signs, discoverable on clinical examination, which are helpful in deciding the question we have just asked.

In examining an individual from the endocrine standpoint, the first thing to do is to note the character of the epidermal structures; the quality and distribution of the hair; the eyebrows in particular merit our attention; the nails and flexures of the body should receive a special note. The presence or absence of sweating; the characteristics of the texture of the skin; and the nature and color of the extremities, should all be noticed.

Having examined the skin, perhaps the next most important step is to make a thorough investigation of the circulatory system. Commencing with the pulse and the state of the brachial artery, passing on to an investigation of the size of the heart, the character of the sounds, and the nature of the cardio-vascular response to stimulation (oculo-cardiac reflex etc.) we shall acquire much information which will help us in determining whether there is any endocrine agent at work which can be regarded as producing abnormal function.

The blood pressure, to the endocrinologist, is of great importance, even if it varies only by small degrees. For example, where the myocardium is sound and the individual in apparently normal health, a blood pressure even slightly but consistently below the normal reading is one which should give rise to suspicion. Exceptions of course arise, and allowing for the fact that there is no

myocardial degeneration, a blood pressure of 100 to 110 systolic, should be regarded as showing some deficiency of a dynamic gland. Equally, a blood pressure higher than normal shows a deficiency of one of the dissimilatory glands, that is to say, those glands dealing with elimination.

The reflexes, particularly the tendon jerks, skin reflexes, more especially the epigastric, and the eyes, should next merit our attention. Brisk tendon reflexes, associated with brisk skin reflexes, are a diagnostic feature of value. It will be recalled that in organic disease of the nervous system, for example disseminated sclerosis, brisk knee jerks are associated with absent epigastric reflexes. If, on the other hand, the brisk reflexes are not associated with absence of epigastric reflexes, I am inclined to think that this sign is useful as showing a generalized parathyroid deficiency, or at least, a deficiency in the fixed calcium in the body.

The temperature should be taken, and the degree of subnormality, or the opposite, noted; the condition of the mouth and of the tongue, its nature and characteristics, are of some value. The atonic, flabby tongue, particularly if associated with gastrointestinal atony, may be regarded by the endocrinologist as of some import, for it is believed by some students that conditions like these are due to parathyroid deficiency.

The urinary and genital systems also require investigation. Amenorrhea, dysmenorrhea, menorrhagia, metrorrhagia and alterations in the sex life as a whole, are all suggestive of various endocrine disturbances. The quantity of urine passed as a rule, compared with that passed on rare occasions, is often of value; for example, patients will sometimes say that at certain hours of the day they pass large quantities of pale-colored urine, and this apart from any bodily disease. That this is sometimes due to pituitary disturbances is acknowledged; in fact, the relation of these attacks to diabetes insipidus is not too far-fetched to mention. Certain information can be obtained in the consulting room from the urine. The acidity or alkalinity, the presence of large quantities of phosphates, and of lime (it is not difficult to estimate this roughly in the consulting room) should all form part of the routine examination when investigating abnormalities of the endocrine apparatus.

When we come to the digestive apparatus, there are many points which demand our

attention. I think it is important that the investigator should realize the part played by the sympathetic nervous system in controlling the gastrointestinal tract, and therefore, the part played by the chromaffin system as a whole. Spastic constipation and the symptoms as the result thereof, would point to some disturbance of the autonomic innervation. Again, the contrast between sympathetic and parasympathetic innervation must be clearly understood if we are to realize the intimate relationship between endocrine disturbances and disturbances of the digestive apparatus as a whole.

As an example of this latter statement, we may refer to the fact that the parasympathetic supplies the esophagus and cardiac end of the stomach; whereas the sympathetic inhibits, and the parasympathetic stimulates such structures as the muscular and secretory glands of the intestinal tract and certain structures derived embryologically from it, such as the liver and gall bladder, pancreas and salivary glands, to mention but a few.

It will be apparent, therefore, that in over-parasympathetic stimulation, we are apt to get spasm of certain of these muscular structures; whereas in over-action of the sympathetic, we get inhibitory results.

When we realize, therefore, that there is a definite relationship between the vagus or parasympathetic and certain of the endocrine glands, and an equally close relationship between the sympathetic and other of the endocrine organs, we shall see how important it is to make a thorough investi-

gation of the intestinal tract, finding out, so far as is practicable, where there is undue rapidity and where there is delay; the condition of the stomach—tonic, hypertonic or normal; the rate of passage of a meal through the gastrointestinal tract, and the action of the sphincters, such as the pylorus and others situated at intervals throughout the digestive canal.

#### Some Conclusions

Sufficient has now been said to show how important it is to gain a clear idea of any variation from normal in the endocrine apparatus. That endocrine abnormalities are able to produce such various signs as headache, palpitation, constipation, to name a few, will show the importance of grasping at even small signs to show which way the endocrine wind is blowing. It is necessary, as indeed it is in every scientific investigation, to make a note of small signs, to classify these signs, and to keep in one's mind clear-cut pictures of any endocrine indications which are present. If the examiner bears in mind the general clinical pictures which are present in what may be called the "full blown" states of under- or over-function, he will gain much help in determining if a commencing abnormality is present or not.

It will be of value also to draw up a chart of endocrine abnormalities, in order that the grouping of abnormal states of skin, tongue, cardio-vascular and urogenital apparatus may fall into definite schemes. If this is done, and clear-cut pictures are borne in mind, it is probable that early abnormalities will but rarely pass unrecognized.

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## A Good Talk

*There are always two to a talk, giving and taking, comparing experience, and according conclusions. Talk is fluid, tentative, continually "in further search and progress"; while written words remain fixed . . . Good talk most commonly arises among friends. Talk is, indeed, both the scene and instrument of friendship.—Robert Louis Stevenson, in "Essays".*

# Exophthalmic Goiter—the Problem of the Endocrinologist\*

By ISRAEL BRAM, M.D., Philadelphia.

AS LONG as closed-minded attitudes prevail in certain fields of endeavor, so long will progress be impeded in those fields. This applies to religion, to politics, and also, unfortunately, to certain phases of medicine. I am criticising, not merely the complete circularity of argument characterizing the Christian scientist or the chiropractor. I refer to the attitude of some gentlemen to whom thyroidectomy is the *sine qua non* in all thyroid enlargements, irrespective of causal relationships and pathologic discrimination. To operate upon a patient with a purely hypertrophic or colloid goiter is nothing short of malpractice. Representative surgeons will admit this. An occasional thyroidectomist, however, will operate upon these patients, and what follows is well known to the endocrinologist. In this category of "touch-me-not-by-the-knife" goiters must be included the hyperplastic thyroid of exophthalmic goiter or Graves' disease, a condition which, unfortunately, is as much sinned against as sinning.

Exophthalmic goiter is *not goiter* and should not be included in the category of purely thyroid enlargements. The disease is no more goiter than is typhoid fever a case of splenomegaly. It so happens that in typhoid fever the spleen is enlarged; and, for that matter, in malaria the liver is enlarged. Do we blame the spleen and liver respectively as the cause of these widespread conditions? Were the thyroid gland situated somewhere within the abdomen, and there became enlarged during the course of the disease we insist on calling exophthalmic goiter, thyroidectomy would be regarded as just as absurd a procedure in the treatment of this disease as would an operation upon the swollen liver in malaria or upon the swollen spleen in typhoid fever.

## Arguments Against Thyroidectomy

There are many valid reasons against surgical approach in exophthalmic goiter, among which are the following:

1.—Approximately twenty percent of all exophthalmic goiter cases present no tangible evidences of thyroid swelling. These instances are frequently the most difficult

to handle, because we here lack the protecting influence of the thyroid swelling which in this disease attempts to immunize the individual against known and unknown toxins originating elsewhere in the body. What shall the thyroidectomist say of these cases? Has he a goiter to operate upon? Is it, therefore, not obvious that removal of redundancy of thyroid structure from an exophthalmic goiter patient presenting a swollen thyroid is an irrational procedure? The disease may be quite as severe after as before operation, and at times even more severe.

2.—Again, what shall we say of those cases of exophthalmic goiter in which, during the course of the disease, there occurs a sudden disappearance of all thyroid swelling, with marked aggravation of symptoms into a tumultuous crisis? Here again we might comment on thyroidectomy as above, pointing out that the spontaneous or induced sudden disappearance of thyroid swelling is by no means conducive to amelioration of symptoms and cure of the disease.

3.—Even thyroid surgeons are constantly faced with postoperative recurrences incident to exophthalmic goiter. This happens rarely in cases where thyroidectomy is really indicated—adenoma or cyst of the thyroid. Postoperative recurrence of non-tumorous goiters in Graves' disease is nature's protest against interference with its corrective processes. Indeed, I am frequently faced by patients in whom two and even three thyroidectomies were followed by regeneration of the mass. These patients, having undergone mutilation or destruction of the thyroid—an organ vitally needful in this disease—find themselves in a predicament far worse after surgical procedures than before. Most instances of complicating insanity, especially the manic depressive form, occur, in my experience, in thyroidectomized patients. The fact that a percentage of these patients feel better for several months after operation is performed is unfortunate, for this result misleads hundreds of others to undergo the same process, with eventual indefinite physical and mental invalidism.

\*From the Bram Goiter Institute, Upland, Penna.

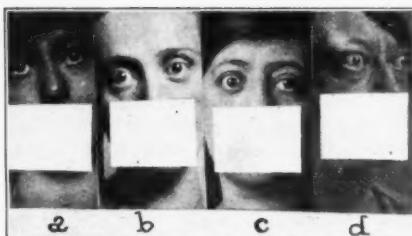


Fig. 1.—(a) Postoperative recurrence of exophthalmic goiter, with return of signs and symptoms within one year following operation; (b) A similar case in which no postoperative improvement occurred; (c) Postoperative recurrence of exophthalmic goiter a year following thyroidectomy; note the unequal exophthalmos; (d) Postoperative recurrence of exophthalmic goiter, the patient in critical condition.

Moreover, myxedema, acromegaly, and other conditions indicating complete disequilibrium of the entire chain of endocrine organs may assert themselves; for is not the thyroid gland the keystone of the endocrine arch? And since the ductless glands are intimately related to the autonomic or vegetative nervous system, not an inch of the body can possibly be made normal as a consequence of indiscriminate thyroidectomy.

4.—Exophthalmic goiter is not uncommonly associated with myxedema in the same individual. This, as aforementioned, is usually instigated by operative interference. But the more telling argument against thyroidectomy in this disease is the fact that many instances of myxedema are superimposed upon patients who have *not* been operated upon. Does this indicate that exophthalmic goiter is *due* to hyperthyroidism? We are not in a position to tell with precision what part the thyroid plays in this disease, but clinical evidences point strongly to two rôles: first, that of protecting the body against toxins; and second, in an endeavor to play this part successfully, the organ undergoes dysfunction. Beyond this we have little, if any, evidence of thyroid participation, unless it be the unusual instance in which pressure symptoms arise from the presence of an enlarged thyroid behind the sternum, in short-necked individuals.

5.—Contrary to the course of events in non-exophthalmic goiters; that is, in goiters unassociated with Graves' syndrome, the swelling in this disease rarely if ever comes first, but is an event which follows many phenomena. First comes an unaccountable restlessness and loss in weight; perhaps evidences of so-called "nervous breakdown"; some heart hurry, with palpitation, undue

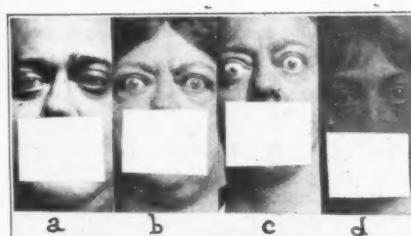


Fig. 2.—(a) Postoperative recurrence of exophthalmic goiter associated with sequential myxedema and acromegaly; (b) Postoperative recurrence of exophthalmic goiter associated with myxedema; (c) A similar case of this sort, with myxedema, in a man; (d) Postoperative recurrence of exophthalmic goiter with manic depressive insanity.

moisture of the skin on little or no provocation, sensations of heat, difficulty in falling asleep, and impatience, irritability, emotionalism and other factors classifiable under the heading of "unusual behavior." This may go on for weeks or months. Even staring eyes may occur at this time, ere evidences of fulness of the neck appear. Enlargement of the thyroid may not be tangible for months, during which time the causative toxins have wrought havoc with bodily processes.

Goiter, in exophthalmic goiter is, therefore, to be regarded, not as the cause, but as the tail-end of the disease; and to operate upon the *resultant tail* as a means of cure is manifestly illogical.

6.—These patients are capable of perfect recovery without any local attention to the thyroid gland *per se*. Since the thyroid swelling is not the cause but a result of the disease, any attempt at effecting recovery by local approach at the thyroid is irrational and unscientific. Should a patient recover from this mode of therapeutics, the result could be regarded as occurring not *because* of thyroidectomy, or of x-rays, or of radium to the thyroid, but *in spite of* these procedures and probably because of the associated broad regime of medical attention so commonly employed by surgeons and roentgenologists who know the limitations of their specialized measures in this disease.

The many hundreds of perfectly recovered patients under endocrinologic care have had no attention given to the thyroid gland itself; and, in my experience, these discharged patients have not only been restored to perfect health, usefulness and happiness, but have stood the test of many years of time.

7.—Unless an individual is congenitally susceptible to exophthalmic goiter, thyroid

extract administration is incapable of producing exophthalmic goiter. This is again a telling argument against the hyperthyroidism theory to explain the cause of the disease, upon which is based the *rationale* of thyroidectomy in treatment. Thyroid extract administration is capable of producing hyperthyroidism, which is a totally different disease from exophthalmic goiter.

#### Differential Diagnosis

There are many points of similarity between these conditions, but the points of difference are so great that it would be well for all physicians endeavoring to diagnose and treat ductless gland disturbances to become thoroughly familiar with the differential diagnosis. Briefly stated, the following points should ever be borne in mind:

##### *Toxic Adenoma or Hyperthyroidism*

- 1.—Patient is usually of middle age.
- 2.—Goiter present years before onset of symptoms.
- 3.—Goiter is essentially adenomatous, often nodular in shape, and usually large, nonpulsating, noncompressible, without thrill or bruit.
- 4.—Exophthalmos and expression of chronic fright rare; no eye signs.
- 5.—Tachycardia not extreme; often materially influenced by sleep and digitalis.
- 6.—Hypertension and myocardial degeneration common.
- 7.—Tremor often absent; if present, is coarse and atypical.
- 8.—Mental symptoms relatively mild.
- 9.—No tendency to crises and remissions.
- 10.—Dermographia often absent; when present, is not intense.
- 11.—Loss in weight comparatively slow.
- 12.—Symptoms may be produced in a normal person by administration of thyroid extract or thyroxin.

Since these patients present a problem that is largely endocrinologic, its solution rests, not with the surgeon, but with the endocrinologist. The problem that he must solve is one that has faced the medical profession for many decades and even today is a foremost topic in medical societies and journals.

The chief obstacle to the solution of the difficulty appears to be the splendidly lowered operative mortality rate incident to thyroid surgery, in representative clinics. This virtue is largely offset by the idea prevalent in the minds of many that *all* patients showing thyroid enlargements should undergo thyroidectomy. Preopera-

tive discrimination of thyroid "lumps" is something which is not given sufficiently serious thought. Not only do we find thyroid hypertrophy and even colloid goiter operated upon, but, what is worse, the hyperplastic swelling incident to exophthalmic goiter is operated upon by the thousand each year, with the consequences that the endocrinologist knows only too well. Also, the temporary improvement following thyroidectomy in these patients, though a merit on the surface, is an obstacle to progress, for it, too, is misleading. Perfect, complete recovery is what the patient craves and should receive in the treatment of exophthalmic goiter, but this is not the result of surgery.

Surgical statistics, though computed by admittedly sincere statisticians, yet are

##### *Exophthalmic Goiter or Graves' Disease*

- 1.—Patient is usually a young adult.
- 2.—Goiter often absent; if present, is of late occurrence.
- 3.—Goiter is essentially hyperplastic in nature, rarely large, usually a symmetrical fulness, often pulsating, compressible, and presents thrill and bruit.
- 4.—Exophthalmos and expression of chronic fright, with characteristic eye signs, are usually present.
- 5.—Tachycardia more pronounced; not materially influenced by sleep and digitalis.
- 6.—Hypotension common; myocardial degeneration may occur late in the disease.
- 7.—Tremor nearly always present and typical.
- 8.—Mental symptoms relatively prominent, with occasional major psychoses.
- 9.—Tendency to crises and remissions.
- 10.—Dermographia constant and usually intense.
- 11.—Loss in weight comparatively rapid.
- 12.—Syndrome not produced by administration of thyroid extract or thyroxin, unless predisposition exists.

hardly dependable. End results are not mentioned—merely immediate operative recovery. Thus clinical cure, the reward for the risk undergone and the scar worn throughout life, is something concerning which we have no information, excepting through the endocrinologist to whom these human wrecks finally make their way.

The problem of the endocrinologist consists of an endeavor on his part to educate both surgeon and internist in the direction of a broader view of the etiology and treatment of exophthalmic goiter. The surgeon must be made to realize that a neat scar and even a resultant clinical improvement does not constitute ultimate cure of the

patient, for relapse is almost sure to follow; and rational therapeutics in a thyroidectomized individual is far more difficult than is the case in a patient whose thyroid had not been tampered with by the knife.

The surgeon must realize that he is entirely justified in operating upon purely neoplastic thyroids, for these are local conditions. Exophthalmic goiter or Graves' disease is, however, not a thyroid affection but a constitutional disturbance, the predisposition to which is lifelong and frequently congenital. It is only through a broad approach, including a correction of dietary, hygienic, sociologic, psychologic and other habits accompanying life's processes, with a view to the stabilization of the neuro-endocrine make-up of the individual, that permanent recovery is possible. This is accomplished, not by a two or three weeks' stay at the hospital, with operation, but through months and occasionally (in badly neglected cases) a year or two of insidious, expertly applied, cooperative effort.

The internist again—he who is often responsible for the presence of this patient on the operating table—must be taught that the nonoperative management of exophthalmic goiter does not consist merely in putting the patient to bed and administering iodine or even quinine. Such a narrow view of the so-called medical treatment of the disease appears to be responsible for the disrepute into which nonoperative attention has fallen

in many quarters. The internist must be more patient with his exophthalmic goiter charge; he must learn to ferret out the faults and foibles of the inherent make-up of the individual, and superimpose a set of habits that would immunize against further inroads of the disease.

In the field of medicaments, the internist should know that what is one's man's meat is another man's poison, and that iodine creates more harm in these patients than any other known factor (outside of surgery) in his armamentarium. Were the internist to devote as much time to the study of these patients as he does to cases of tuberculosis or diabetes, there is no question but that, within the next ten years, his results in the management of this disease would lead to the conclusion that thyroidectomy as a means of treatment should be prohibited by law.

Finally, may I urge that a widespread movement be undertaken in the investigation of the end results of thyroidectomy as a treatment of exophthalmic goiter, and that this movement should also include the investigation of the end results of the treatment advocated by representative endocrinologists. Let me predict that impartial figures thus procured would be an eye-opener and would revolutionize and standardize the treatment of this most interesting disease in medicine—Grave's disease.

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## The Thyroid Gland and Menstrual Disorders

By MAXIMILIAN KERN, M.D., Chicago.

THAT a connection exists between the thyroid gland and the ovary has long been known; clinical findings are daily strengthening this observation and adding concrete proofs to it. Bram<sup>1</sup>, in his book on Goiter says that Weil describes two cases of sexually normal women in whom, following extensive thyroidectomy, menstruation became irregular and finally ceased; both developed the symptoms of a true menopause but both also recovered under treatment with thyroid extract. Jalecowitz<sup>2</sup> has recently described a case in a woman, aged 28 years, who, following a thyroidectomy for goiter, showed every month a vicarious hemorrhage at the site of the operation. In this case the thyroid was not completely extirpated and normal menstruation was

re-established 5½ months after the operation.

These examples show that alterations in the thyroid function are capable of reacting upon the ovarian function and disturbing menstruation. On the other hand, as we shall presently see, disturbances in the ovarian function are also capable of affecting the thyroid function.

### Normal Menstruation and the Thyroid

Bram<sup>1</sup> notes the fact that while, at the onset of puberty, the thyroid enlarges, in both the male and female, the enlargement in the female at the menstrual periods and at all important sexual manifestations is very common. He also states that the normal menopause is often profoundly influenced by the condition of the thyroid

gland and that many of its symptoms are apparently due to an alternating hypo- and hyperfunction of this organ.

In textbooks and in the literature, there are but few allusions to the connection between the thyroid, the ovaries and menstruation. Most authorities agree that the thyroid increases in size at the onset of menstruation at each menstrual period and at sexual crises during the genital life of the female.

There is a certain amount of disagreement in regard to other physiologic changes involving the thyroid and parathyroids, due to normal menstruation. Wiltshire<sup>4</sup>, for instance, considered from his investigations that the basal metabolism was not altered during menstruation; but Wakeham's observations on 24 women showed that there was a distinct fall in the basal metabolism during or immediately following menstruation. Lanz<sup>5</sup> found that the basal metabolism was increased toward the end of the interval and during the premenstrual period and that it reached its lowest point during the postmenstruum and at the onset of the interval.

My personal observation regarding basal metabolism during menstruation is based upon findings in a series of twenty-five cases. In studying the basal metabolism in these patients for the purpose of determining the relation of their obesity to metabolism, I discovered that while there was an average of minus 30 which could be raised to normal or even as high as 20 plus by the administration of thyroid extract, under normal conditions, there would again be a fall in the basal metabolism during and following menstruation, in spite of the thyroid medication. On the other hand, in the same series of patients, I found the basal metabolism raised between 20 and 30 percent immediately preceding menstruation. This conclusion seems to be in complete accord with the findings of other writers and lends itself to a logical correlation between thyroid function, as expressed in basal metabolism readings, and menstruation.

As to whether this rise in the basal metabolic index is due to some endocrine factor, *per se*, or to the usual state of 'emotionalism' which is characteristic during menstruation, I am not prepared to draw any definite conclusions. It would probably be of no clinical significance if we were to trace emotionalism in general to an endocrine disturbance, in spite of the fact that it is well known that there is an increased metabolism read-

ing during a state of excitement or emotion. Such a reading, however, cannot be construed as basal, in view of the fact that it lacks in constancy and is not a true expression of the metabolic function.

The parathyroids are known to be concerned in maintaining the calcium level in the blood serum. From experimental work by Sharlit and his associates<sup>6</sup> it was found that there was a rise in the concentration of calcium in the blood at the approach and onset of menstruation. This observation was confirmed by Kylin's<sup>7</sup> findings. Allen and his associates<sup>8</sup> also showed that the administration of parathyroid extract decreased the clotting time and the bleeding time in women with excessive menstruation; that is to say, that the parathyroid hormone checked very profuse and long-continued menstrual hemorrhage, although these investigators could not find any concomitant increase in the blood serum calcium. Maurer<sup>9</sup> has recently shown that there is an alteration in the iodine content of the blood during menstruation.

#### The Pathologic Thyroid and Menstrual Disorders

Leaving aside these more or less physiologic aspects of the thyroid and menstruation, let us proceed to discuss the connection between obvious thyroid dysfunctioning and its connection with menstrual disorders.

McCarrison<sup>10</sup> and other writers remark that, in cretinism, the uterus and ovary may remain infantile and that menstruation may never be established. Gardiner-Hill and Smith<sup>11</sup> observed 9 cases of cretins, 7 of whom had received thyroid treatment; 5 of these had menstruated, the average age at menstruation being 16 years—much higher than the average. This series (as well as many cases of my own) shows that when thyroid treatment is begun early, even in cretins, menstruation may be established and that it may be regular. If there is no thyroid therapy in cases of cretinism, menstruation is likely to be absent or else scanty or irregular.

Most writers on the subject agree that myxedema is usually accompanied by menorrhagia. Starr<sup>12</sup>, Kirk<sup>13</sup> and others observed this connection as early as 1893, and both McCarrison and Bram in their more recent writings express a similar opinion. However, both amenorrhea and menorrhagia have been reported associated with myxedema, and this agrees with my own experience.

Gardiner-Hill and Smith state that there seems little doubt that, where myxedema

develops before the menopause, it is frequently accompanied by menorrhagia and only rarely by amenorrhea. These writers classify the cases into three types:

(a) Myxedema occurring before the natural menopause.

(b) Myxedema occurring after the natural menopause.

(c) Myxedema occurring after premature menopause.

In class (a) the great majority (78 percent) suffer menorrhagia; in class (b) menstruation has usually been regular up to the time of the menopause; as regards class (c), myxedema is observed to be a common sequel of the artificial menopause, whether induced surgically or following roentgen-ray treatment or other cause. Frequently castration is followed by hypertrophy of the thyroid, and Thorek<sup>14</sup> shows an example of an enormous hypertrophy of the thyroid following castration in a dog.

#### Goiter and Menstruation

Hoskins<sup>15</sup> thinks that, in districts where goiter is endemic, a large proportion of the females have scant menstruation as well as other menstrual disorders.

Hertzler<sup>16</sup> says that there usually is disturbance of menstruation in patients with goiter.

In 90 cases of adolescent goiter, followed by Gardiner-Hill and Smith<sup>17</sup>, they found that the character of menstruation tended to vary inversely with the degree of thyroid activity. If there was little or no thyroid disturbance menstruation was regular. Menstruation was regular and normal in approximately half the cases of colloid goiter observed by these writers, whatever the degree of thyroid activity present, and in the majority of the other half menstruation varied inversely with the thyroid activity. When hyperthyroidism was present, menstrual periods were usually delayed and irregular and the discharge was scanty or even absent. In cases where there was clinical evidence of hypothyroidism there was a tendency to menorrhagia. My own observations are in exact agreement with the findings of these investigators. The general rule observed in all thyroid disturbances which were associated with menstrual irregularities was that, with an overactive thyroid, the menstruation was delayed and scanty, but with an underactive thyroid menorrhagia was usual.

Amenorrhea is usually an accompaniment of exophthalmic goiter; clinical reports show this menstrual disturbance in more than half the cases. Menorrhagia is rare with exophthalmic goiter. In hyperthyroidism without exophthalmos, menstruation is normal in a high percentage of cases and the minority show a tendency to amenorrhea.

In simple adenoma of the thyroid, in which there is but little disturbance of the gland functioning, menstruation is generally normal and regular in the majority of cases; but when there is a disturbance in menstruation it is usually of the menorrhagia type; that is to say, that the type of menstrual disturbance always varies inversely with the degree of thyroid functional activity.

#### Personal Cases

In my own records I find a number of cases in which menstrual irregularities were found associated with thyroid dysfunctioning. The following list contains the cases that I have been able to follow for some years so that the course of menstruation was observable. These cases I have arranged in two series according to the time the patients were first observed by me—prior to or after the establishment of menstruation or at least the age of normal puberty:

#### A.—*Pre-pubertal Cases*

##### 1.—Myxedema

(a) Cases in which no thyroid medication was given.....	4
Failed to menstruate or had scanty menstruation.....	3
Menstruated more or less regularly .....	1
(b) Cases in which thyroid treatment was regularly given early .....	5
Failed to menstruate.....	1
Scanty menstruation.....	1
Fairly normal menstruation....	3

#### B.—*Post-Pubertal Cases*

##### 1.—Adolescent Goiter:

Normal menstruation.....	6
Irregular menstruation.....	2

##### 2.—Colloid Goiter:

Normal menstruation.....	1
Irregular menstruation.....	1

##### 3.—Myxedema:

Normal menstruation.....	4
Irregular menstruation.....	7
(b) Of these (7) patients there were relieved by thyroid medication .....	5

4.—Hyperthyroidism without exophthalmos:	
Normal menstruation.....	5
Amenorrhea in.....	1
Menorrhagia in.....	3

As a general rule I have found that thyroid extract, either alone or combined with corpus luteum extract, has relieved patients with menstrual irregularities of any type, independently of the underlying cause of the irregularity.

#### Conclusions

From my experience I consider that in untreated cretinism menstruation is either absent or unduly delayed. When thyroid therapy is established early and kept up continuously, the prognosis is rendered more favorable.

In hyperthyroidism, either in young or adult patients, delayed, scanty or irregular menstruation may be expected; while in hypothyroidism menorrhagia is more likely to occur.

Mxedema occurring before the natural

menopause is likely to be accompanied by menorrhagia.

#### References

- 1.—Bram I.: "Goiter", 1924, p. 23.
- 2.—Jalcowitz, A.: *Deut. Zeitschr. f. Chir.* 1926: exxviii: 101.
- 3.—Wiltshire: *Amer. Jour. Obstet. and Gynec.* 1921: ii: 489.
- 4.—Wakeham, G.: *Jour. Biol. Chem.* 1921: lvi: 555.
- 5.—Lanz, W.: *Zeitschr. f. Geburtsh.* 1925: lxxix: 133.
- 6.—Sharlit, H. and Associates: *Arch. Int. Med.* 1927: xxxix: 780.
- 7.—Kylin, E.: *Zeitschr. f.d. Ges. exper. Med.* 1924: xlvi: 50.
- 8.—Allen E. and Associates: *Am. Jour. Obstet. and Gynec.* 1927: 156.
- 9.—Maurer, F. E.: *Arch. Gynaec.* 1927: cxxx: 70.
- 10.—McCarrison, R.: "The Thyroid Gland", London, 1927, p. 186.
- 11.—Gardiner-Hill, H. and Smith, J. F.: *Jour. Obstet. and Gynec. of the British Empire.* 1927: xxiv: 701.
- 12.—Starr, Allen: *Med. Record*, N. Y., July, 1893.
- 13.—Kirk, R.: *Lancet*, London, 1893: ii: 743.
- 14.—Thorek, Max: "The Human Testis", 1924, p. 456.
- 15.—Hoskins, R. G.: "Endocrinology and Metabolism", Vol. 1, p. 923.
- 16.—Hertzler, A. E.: "Diseases of the Thyroid Gland", 1922, p. 183.

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## The Influence of Endocrine Diseases on Nutrition and Basal Metabolism

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CONTRARY to popular belief, a basal metabolism test is not intended to measure all disturbances in metabolism, such as disturbances in the metabolism of sugars (diabetes) or of fats (acidosis), or the failure to utilize mineral salts (rickets) or disturbances in the elimination of the nitrogenous end-products of protein breakdown (nephritis) or the varied forms of disturbances of nutrition which result from dietaries deficient in vitamins. A basal metabolism test does, however, measure a disturbance in the rate of utilization of one of the food stuffs, namely oxygen.

The basal metabolic rate is that rate of oxygen utilization and energy-loss which occurs when the body is producing heat at its lowest rate; that is, when the subject has been mentally and physically quiet for about one-half hour and when the gastro-intestinal tract contains no absorbable food.

In contradistinction to the basal metabolism, the *total metabolism* of the body is the consumption of oxygen and the output of energy for 24 hours, which includes all the losses of energy caused by work, emotional stress, the specific dynamic action of food and the basal metabolism. The specific

dynamic action of food is the effect of the absorption of food in stimulating the cells to take up more oxygen than they use under basal conditions. Proteins have a marked action in this respect, fats less, and carbohydrates least, the loss from the rise in the metabolism being sufficient to cause a loss of 33, 11, and 5 percent, respectively, of the calories of the food-stuffs thus consumed. DuBois calls this loss or waste of calories "the cost of digestion".

Normal basal rates vary with age and sex, being higher in males than in females and in the youth than in the adult. (See Table 1 of normal rates. There are two other sets of normal tables widely used in this country but their agreement with each other and with Table 1 is comparatively close.)

#### Measurement of the Basal Rate

A measurement of the basal rate is a comparatively simple procedure. The device here illustrated is a modification of a method previously described by the writer<sup>1</sup>.

It has been proved by the researches of Rubner, Voit, Lusk, Atwater, Benedict, and others that, for each liter of oxygen burned in the body at the respiratory quotient of

Table 1  
*Average Rates of Persons in Health, in  
 Calories per Hour per Square  
 Meter Body Area  
 (From Aub and DuBois)*

Age	Males	Females
6-8	58.0	58.0
8-10	54.0	54.0
10-12	52.0	50.0
12-14	50.0	46.0
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.5
30-40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60-70	36.5	34.0
70-80	35.5	33.0

.82, there is a heat production by the body of 4.825 calories\*.

To arrive at the hourly output of energy, it is only necessary to determine the time required to consume a liter of oxygen and then to translate this amount into heat units per hour or per 24 hours by multiplying the number of liters so consumed by 4.825. Normal rates, as here given in Table 1, are stated in terms of calories per hour per square meter of body area, the body surface area being determined in square meters by means of the body area table prepared from the height-weight formula of DuBois (see Fig. 1). After we have determined the patient's body area from his height in inches and nude weight in pounds—this being done without calculation—it is only necessary to read—also without calculation—from a chart (see Fig. 2) the number of calories per hour per square meter given off by this patient, that is, his rate of metabolism.

The timing device is contained in the apparatus and the usual table at the bed-

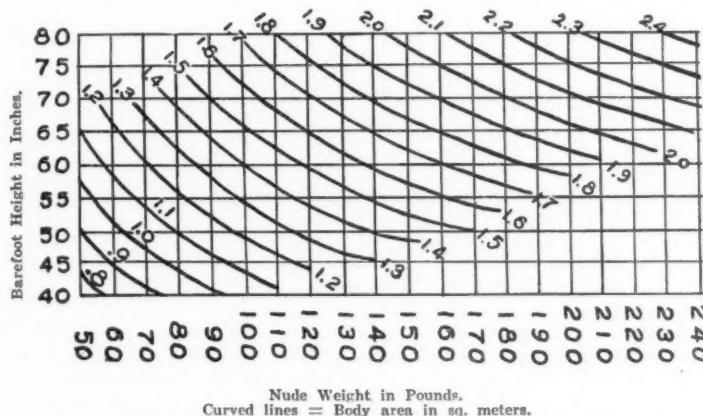


Fig. 1.—For Reducing Patient's Height and Weight to Square Meters of Body Area.

\*Under basal conditions the amount of carbon dioxide eliminated by the body is about 820 cc. for each 1000 cc. of oxygen consumed. This gives a respiratory quotient (R.Q.) of 820/1000 or .82. In extreme acidosis, the R.Q. may fall as low as .68. At the R.Q. of .82, oxygen has a heat value of 4.825 calories per liter, whereas at the R.Q. of .68, as seen in rare instances of acidosis, this heat value may fall to two percent below 4.825, thus making an error in the calculation of a possible two percent. Because this error is so insignificant, the determination of the R.Q. by the old-time elaborate chemical examination of expired air (the so-called Tissot method), which was calculated to determine the exact heat equivalent of oxygen, has long since become obsolete. The method of determining the heat output by assigning the heat value of 4.825 calories to each liter of oxygen consumed by the body is universally accepted as correct in principle and is remarkably exact, for the reason that the R.Q. rarely varies very widely from the value .82.

side is replaced by the framework of the apparatus which is adjustable to the height of the bed.

All normal basal metabolic rates are based on the amount of oxygen consumed per unit of time, such oxygen being assumed to have been measured under the standard pressure used by the physicist for measuring gases, namely, 760 mm. of mercury. If the barometric pressure at the time and place of making the test varies from this standard of 760 mm. Hg.—and it always does—then, before the rate of oxygen consumption of the patient can be

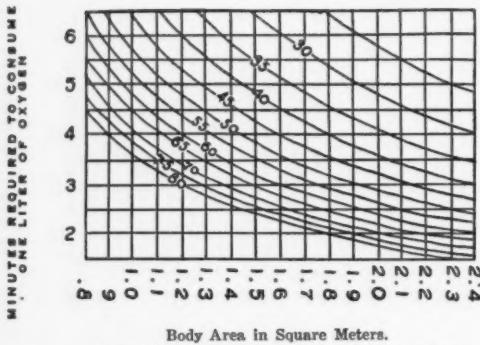


Fig. 2.—For Reducing Stop-Watch Time and Patient's Body Area to Calories per Hour per Square Meter.

compared with the normal rate, the volume of oxygen so consumed must be translated by calculating the volume it would occupy at 760 mm. Hg.

To eliminate this need for a barometer and the foregoing calculations, the gauge was devised to be used for measuring the oxygen in a tube of one liter volume and under a pressure of 760 mm. Hg., this standard pressure being admitted into the tube in addition to, or over and above, the barometric pressure present at the time and place of making the test, namely, the room barometric pressure. Then, at the appropriate time during the test, this pressure in the liter-volume tube is discharged into the instrument until the gases within the tube again return to the same room pressure. Thus it is obvious that all the gas admitted into the liter tube has discharged itself by the force of its own pressure into the breathing chamber of the apparatus.

To calibrate the gauge to show a pressure of 760 mm. Hg. above the room pressure is a simple laboratory procedure and the gauges used for this purpose have remained accurate to within one-half of one percent throughout a period of seven years of daily use.

It must be remembered that an increase in temperature causes gas to expand in volume. For this reason, there must be a standard temperature at which the gas is used; otherwise, another calculation would be necessary to correct this change in volume, as in the case of barometric variations. With the gas in the tube at the temperature of 0°C., the 760 mm. Hg.

pressure position of the indicator would be at a given point on the dial, while at 10°C., 20°C., etc., it would occupy positions indicating slightly increased pressures (27.8 mm. Hg. for each 10°C. rise in temperature). These points on the gauge are likewise easily located at appropriate distances along the edge of the dial. Thus, without the necessity of calculation, the gauge automatically and simultaneously corrects for barometric and temperature variation.

The aqueous tension effects are thus also eliminated, since the gas is measured as dry oxygen.

It might be thought that a mixture of the oxygen with air would effect the result of the test, but it is readily understood that this has no effect when it is remembered that the liter of oxygen, even if mixed with air, simply distends the bellows by one liter of volume and the patient (utilizing only oxygen) would reduce it by the same volume—one liter. Since the only gas that the patient can use is oxygen, the sole object for which the test is made is thus accomplished, namely, to measure the time required for the patient to reduce the volume of the bellows by just one liter of gas.

Moreover, the procedure required the determination of two factors, the time and the volume of oxygen. The time factor can be determined with any degree of accuracy desired, for the reason that the clock mechanism used is the same in principle, in parts, and in adjustment, as that of any accurate, standard eight-day clock. The oxygen-volume factor is determined with a degree of refinement far greater than has any meaning in this work, the maximum variation being equal in volume to the oxygen consumed by the patient in about one-fourth of a second, out of the five to seven minutes used for the test.

Since these two factors, the time and the volume, are the only data to be read from the instrument, it is clear that, when these two factors are measured correctly, any error creeping into the final calculation of the results is from some source outside the instrument, and the reason for the error should be traced to the proper source and not attributed to the instrument. Loss of oxygen through the nose, because of a carelessly applied nose clip, is a common source of error, but this loss need never occur if instructions are followed and care is used in applying the clip to the nose.

### Sources of Variation

1.—When psychic influences are eliminated and the subject is kept quiet, the metabolic rate itself varies in a given patient, within about two percent, from one test to the next.

2.—There are three different sets of so-called "normal-rate tables", each of which differs from both the others. The normal tables of standards established by Aub and DuBois are used in connection with the method here described. Those of Benedict, used rather widely in this country, disagree with the Aub and Dubois standards by as much as 10 percent in some parts of the tables.

Thus it may be that a subject may consume 200 cc. of oxygen per minute from each of two types of instruments; but in the one, the tables accompanying the instrument may indicate that he should normally consume 196 cc. per minute; that is, that his 200 cc. per minute of oxygen consumption is two percent *above* his normal rate; while the tables accompanying the other may say that he should consume 212 cc. per minute; that is, that the 200 cc. he consumed is six percent *below* his normal rate. In other words, even though he consumed identical amounts of oxygen from the two instruments in the same length of time, he is assigned "plus two percent" by one instrument and "minus six percent" by the other—rates that disagree merely because the tables disagree. It is, therefore, useless to try to get two instruments to "check" when two different tables of normal rates are used. The accurate check is to determine whether or not the patient consumes the same amount of oxygen per minute from each instrument. Beyond that, the instruments are not to be blamed for failure to "check" in percentages of disagreeing normal rates. It seems to be a favorite pastime of the novice in measur-

ing the metabolic rate to try to make the instrument of his choice check with that of some other make, and though he should always take into account the cause of disagreement, he almost never does so.

3.—To have the patient stay in the hospital all night preparatory to the test the next morning is a useless procedure. Thirty minutes of rest after the muscles become quiet is sufficient time for the tissues to catch up with the oxygen demands made by the exercise. The patient usually comes into the doctor's office in the morning or afternoon from six to fourteen hours after the last meal (a longer period is unnecessary), lies down for thirty minutes and is then under basal conditions proper for the test.

4.—Mechanical sources of error have been discussed. The volume of gas used with the type of apparatus here described may vary (+) (-) one-tenth of one percent. The variation in the time factor is negligible. The variation in the body-area factor is about one and one-half percent, for normally shaped bodies.

5.—Psychic disturbances are the source of variations ranging from 5 to 15 percent or more. Fear is the common cause and disappears when the first test is finished. If the second test, which is begun immediately after the first, is higher than the first, it should be checked by a third. If the nature of the test is explained to the patient the variation

seen in the first test is usually eliminated

6.—The patient should breathe to the completion of expiration at the end of the test as at the beginning. A consideration of the tracing itself and of the method of determining the oxygen volume consumed will make it clear why this is true. (See Figure 4). In the case of very irregular breathers this may be a source of error amounting to (+) (-) five percent, but it is negligible if the breathing is regular. This error is a characteristic of the patient

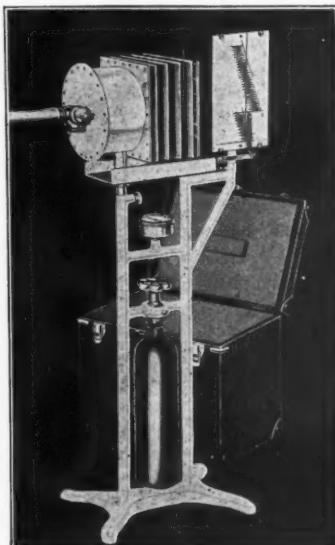


Fig. 3.—The apparatus, containing no fluids or other contents which might spill may be carried to the patient's room in the hospital, or in any position, either assembled or packed in a small sized carrying case, to the patient's home.

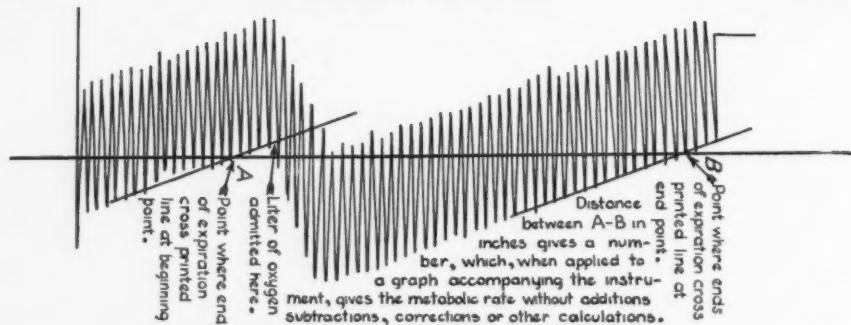


Fig. 4.—Photograph of tracing sheet illustrating how time and volume are indicated. At point A the bellows to which the tracing pen is attached has a certain degree of expansion. At point B it has the same degree of expansion. In the interval between these two points the operator has disturbed this degree of expansion by one liter (injected by the measuring device on the apparatus), while the patient has disturbed this degree of expansion by the same amount, namely, one liter. Thus the operator knows that one liter has been consumed in the interval from A to B, the latter distance in inches being the measurement of the time factor in minutes.

rather than of any particular type of instrument.

#### Pathologic Variations

As in the measurement of any physiologic quantity, the limits of variations for the basal metabolic rate for normal persons have been arbitrarily set. A basal metabolism rate ranging between minus 10 and plus 10 is considered to be within normal limits. Anyone with a rate slightly above the plus 10 percent limit should be requested to return for subsequent observation. In the case of an individual with a rate below the minus 10 percent, other definite signs of hypothyroidism should be carefully watched for before the diagnosis is made. In fact, the definite clinical signs of hypothyroidism are practically never seen unless the rate has descended to at least approximately minus 25 percent.

Certain diseases, especially of the thyroid and of the pituitary glands, which in some instances are diagnosed with considerable difficulty because of their irregular clinical manifestations, produce a distinct change in the rate of oxygen consumption, and this change should leave no doubt as to the diagnosis.

In what patients, other than those with thyroid and pituitary disturbances, may the basal metabolism rate be altered?

In the following conditions the metabolic rate is raised:

- 1.—Pernicious anemia (as high as plus 40 percent).
- 2.—The leukemias.
- 3.—Typhoid fever (mainly because of the increased temperature).
- 4.—Pregnancy (about plus 20 percent at term).

5.—All fevers (a rise in metabolism of from plus 5 to plus 10 percent for each Fahrenheit degree rise in temperature).

6.—Hyperthyroidism (from 20 to 40 percent in mild cases, 40 to 60 percent in moderate cases, and 60 to 100 percent or more in severe cases).

7.—Hyperpituitarism; i.e., gigantism or acromegaly (up to plus 40 percent).

8.—Diabetes (up to plus 20 percent in early cases, although below normal after the subject becomes emaciated).

9.—Cardiac decompensation (up to plus 40 percent).

In the following conditions the metabolic rate is reduced:

1.—Myxedema and cretinism; i.e., hypothyroidism (as low as minus 35 percent).

2.—Froelich's syndrome of pituitary origin (about minus 25 percent); although in Froelich's syndrome of the eunuchoid type, from which it is most often clinically indistinguishable, the rate is normal.

3.—Pathologic obesity of hypothyroid or pituitary origin. (In simple obesity—the obesity of laziness and of big eaters—the rate is normal).

4.—Extreme cachexia, as in tuberculosis, diabetes, prolonged starvation, etc. (as low as minus 30 percent).

5.—Individuals in perfectly normal health, whose heart rates are low, (as low as 50 beats per minute), may show a metabolic rate as low as minus 20 percent.

6.—Addison's disease (about minus 30 percent).

The important point to remember is that these conditions rarely coexist with thyroid or pituitary disorders, and even if such a

combination should be present, the thyroid or pituitary disorder would be easily recognized or demonstrated by more obvious means.

The signs and symptoms of hyperthyroidism are more often obscure than clear-cut. In diagnosing hyperthyroidism without the basal metabolic test, the difficulty lies in the fact that no single sign or symptom of that disease is constantly present; and, conversely, even if any sign or symptom by which this disease is diagnosed is present, it may have some other cause. On the other hand, an increased basal metabolic rate is the one and only constant feature of the disease; and again conversely, no other disease causes an increased basal metabolic rate of the degree seen in hyperthyroidism without being easily recognized by its own signs and symptoms. In other words, the basal metabolic determination is not used in cases which are clinically cases of hyperthyroidism; it is used to test *all* patients who have no definite clinical picture of any particular disease, in the belief that it may point to hyperthyroidism.

#### Nutrition and the Metabolic Rate

Anyone who has experienced changes in body weight will agree that there is a certain weight of the body or state of nutrition at which one feels and looks physically more fit than at any other and at which, also, one should be most efficient.

Visceroptosis of the undernourished hypochondriac or neurasthenic is more satisfactorily treated by fattening the patient than by any other form of treatment. Patients who have taken too little food for one or another reason for a prolonged period eventually become victims of chronic inanition and require intelligent management of their diet before they can be brought back to their former normal weight. On the other hand, overnourished or obese individuals are regarded as dangerous risks by all life insurance companies, because of the frequently associated conditions or sequelae of high blood pressure and diabetes. Dysmenorrhea and even amenorrhea in obese women is frequently best treated without remedy of any kind other than a reduction of body weight.

To a large number of people, especially of women, the disfiguring effect of an oversupply of adipose tissue is the dread sign of advancing years, one that they would gladly evade if they but knew the secret of some sure and easy method of doing so.

It is clear from the foregoing that the control of the state of nutrition of the body should come well within the limits of the physician's knowledge and duty.

Disturbances in nutrition in greater or less degree are observed every day, often in combination either with a change in the basal metabolic rate or with some disease of the endocrine organs or both. The part, however, which the endocrine glands and the basal metabolism play in the process of nutrition is one phase of medical education in which, for some reason, misinformation has long been more popular than truth. In fact, any medical man, possessed of even a moderate sense of humor, can entertain and surprise himself by the hour with the great variety of novel ideas that can be uncovered on the subject of the endocrine organs, and especially of the effect that they have on the basal metabolic rate and on nutrition.

One author may state that the metabolic rate can be measured to within a fraction of a percent; another, that no metabolic rate determination is closer than ten percent to the true condition; another, that any patient with a minus one percent or any rate below zero is not normal and ought to have regular doses of thyroid extract; while another will say that one should consider minus ten to be within normal limits and that another ten percent should be allowed for possible error in making the test.

One claims that obesity is due to disease of the pituitary gland; another, to disease of the sex glands; and another, to a subnormal action of the thyroid gland.

Another patient with a toxic goiter and a plus 65 percent rate finds, after thyroidectomy, that his metabolic rate has dropped to minus five. He blames the surgeon for having taken out too much of the gland and he starts taking thyroid extract to increase his basal metabolism.

When a patient gains weight, following the menopause or castration, the gain in weight is said by one to be due to an absence of the sex gland hormones; by another, to a normal diminution of sexual exercise; and by another, to a reduced basal metabolism.

One internist presents a series of cases of "mild" hypothyroidism. Symptoms, such as a low basal metabolism (-10 to -15 percent), low heart rate, low blood pressure, fatigue, undernutrition and occasionally dry

skin, are reported as being distinctly benefited by the administration of thyroid extract, this therapeutic result being the only test by which such cases can be distinguished from those of typical neurasthenia.

Another internist reports the same type of case, especially pointing out the fact that a patient with a low basal metabolic rate may not have a low rate according to one of the other tables, or standards, of metabolic rates, and that thyroid extract administered to *anyone* will cause a moist skin, an increased basal metabolic rate, an increased heart rate and increased blood pressure. The clinical test whereby the latter observer concludes that these are not cases of mild hypothyroidism is the permanent clearing-up of the symptoms on a regimen calling for a regulated mode of outdoor life, with several months of forced feeding, with moderately hard physical exercises, and the application of small, regulated and increasing doses of actinic rays or direct sunlight.

Still another internist may report that he frequently observes cases in which, at the same time, in the same patient, both diseases, hypo- and hyperthyroidism co-exist.

#### Fallacies of Metabolism and Nutrition

Although I have no figures or statistics to prove the point, it is my conviction, after eleven years of discussing this subject with medical men, that when the subject of nutrition is raised for discussion, 99 out of every 100 medical men are ready to cite dozens of everyday observations of their own to prove that an increased food intake for those who seem to be naturally underweight or a decreased food intake for those who seem to be naturally overweight will not cause the thin to gain nor the obese to lose weight. It is certainly not far from the truth to say that, of all remedies, dieting is the most popularly misapplied, and that day after day hundreds of persons who are in need of intelligent direction and control of body weight are abandoned, either to their "glands" or to the tricks of the beauty doctor.

So convinced is the average doctor by his experience that his argument is almost stereotyped. He recalls the instance of a certain woman who eats almost nothing and yet keeps right on gaining weight. When asked of what material all this weight is made, he confesses entire ignorance of the chemistry and arithmetic of nutrition, hazarding only a guess that it must be the

fault of her sex glands, her metabolism, her pituitary gland or something else, and there either lets the matter rest or breaks out in another place with more "personal observations". He has never, even by the crudest method, measured the 24-hour food intake, or considered the kinds of foods, or the number of meals per 24 hours that her body requires. He has made no note or measurement of her rate of metabolism per 24 hours to check against this, but he just "knows" that her weight increases on almost nothing. His argument is too unworthy of a scientific man to be called a personal observation, but this situation is recited merely to illustrate how universal is this lack of a practical working knowledge of the chemistry and arithmetic of nutrition and how conveniently vague references to the metabolism or to the endocrine glands are made to explain every physiologic mystery.

No one can justify such a chaos of misinformation. It is true that mere theory and speculation have characterized our textbook stories of the endocrine glands with their supposed effect on the mental, sexual, social and physical development and their vicious circle of intereffects. These stories are partly true, and much is still in doubt, but the part the endocrine glands play in the practical, usable medical facts relating to the nutrition and metabolic rate is as definitely known as the chemistry or mathematics or any phase of the "science of nutrition"—for nutrition is a science.

How willingly everyone commits himself on this subject even in the absence of any kind of accurate knowledge; how well pleased he is with his own interpretation of these mysteries; and how this interpretation in turn contributes to the overuse of bad remedies and to the misuse of good ones, the few instances here cited are totally inadequate, both in number and kind, to illustrate. This statement is based on the conflicting answers picked up from various sources, to the following simple questions.

It will be noted that these questions do not involve theory but merely plain yes-and-no answers, in terms of facts which have been many times proved by ordinary laboratory procedures. The few persons to whom the answers are familiar will in every instance be those who have come to know by experience the wonderful therapeutic value of food and food control, than which the

entire pharmacopeia contains no remedy of greater healing virtue.

**Questions on Metabolism and Nutrition**

1.—*What is the coefficient of absorption of food in the form of a mixed diet?* How is the coefficient affected: (a) if the amount of food ingested is 50 percent, or even 100 percent, above the amount usually taken; (b) if the intake of food is in excess of the needs of the body; (c) if the food is forced upon a person in spite of a distaste for the food? By what pathologic conditions of the gastrointestinal tract is this coefficient influenced? (If you believe that some individual is not normal in this respect, what proof have you, not theoretical, but in actually measured quantities of known substances leaving the body?)

2.—*What is the law of conservation of matter? What is the law of conservation of energy? Do these laws hold true in the nutrition of the body?*

3.—*What is a maintenance ration? On a maintenance ration of 125 Grams protein, 60 Grams fat, 350 Grams carbohydrate, in what form and how does this complex material eventually leave the body, and approximately what total weight would it then have in grams?*

4.—*What is the caloric value of the above ration? What approximate distribution of these calories would you make in your daily mode of life in the form of: (a) body heat, or basal metabolism; (b) mechanical energy, or work; (c) psychic, or emotional expenditures; (d) specific dynamic action of this amount of food; (e) loss as unabsorbed food along with feces? What would be the total metabolism?*

5.—*How would these items of caloric expenditures be changed if you were a patient with hypothyroidism with a basal metabolic rate of minus 32 percent? What would be the total metabolism in this case? How would these caloric expenditures be changed if the patient had hyperthyroidism with a basal metabolic rate of plus 50 percent? How would this disease affect the total caloric output?*

6.—*What is the law of definite proportions? Does it hold true in the chemistry of food utilization by the body? For its complete utilization in metabolism, does each molecule of a given protein require the same number of oxygen atoms as are required by every other molecule of that same protein? Does this hold true for carbohydrates? Fats?*

7.—*If the molecules of food supplied to the body during each 24 hours are all used up for oxidation purposes before the 24-hour period is up, will oxidation then cease? How will it be maintained? How predict what the loss in weight will be?*

8.—*If the molecules of food supplied to the tissue during each 24 hours are not all used up for oxidation purposes at the end of the 24-hour period, how can the amount in excess of the 24-hour needs escape from the body? This excess will be stored as what: (1) if the body has already attained its full muscular development; and (2) if the body has not reached its full muscular development?*

9.—*If a patient on a weight-reducing diet expends a total of 3000 calories per day and consumes only 2500 calories per day, how many days will be required for the loss of a pound of weight, provided that the body tissue used up is 20 percent muscle and 80 percent fat (muscle = 600 calories per pound)?*

10.—*If certain conditions, such as emotional stress, hard labor, or certain diseases of the endocrine glands, cause the body to demand more oxygen, what is the effect on body weight if the food intake remains the same? By what means can the body be made to demand more oxygen so as to effect the desired loss in weight? If the body is made to demand more food without increasing the oxygen utilization, what is the effect on body weight? By what means can the body be made to demand more food?*

11.—*In what way does hyperthyroidism (often, but not always) cause loss of weight, in spite of increased food intake? It is the change in the basal metabolic rate or the change in the total metabolism which is more to blame? In what way does hypothyroidism (often, but not always) cause gain in weight, in spite of decreased food intake? Is the basal metabolic rate or the total metabolism more to blame?*

12.—*Is there any method, other than forcing the body to use more oxygen or less food, by which body weight may be reduced? Is there any method, other than by forcing the body to take more food or less oxygen, by which the body weight may be increased?*

13.—*What diseases of the endocrine glands cause a change in the basal metabolic rate? In the total metabolism? How is this change proved?*

The above questions are given in this sequence in order to lead the reader by his own knowledge of facts to the following conclusions:

#### Conclusions

1.—Contrary to almost universal belief, food in the form of a mixed diet, regardless of how excessive the amount ingested, or the lack of hunger, or appetite, or distaste for it, and regardless of the body's need for it, will be absorbed, up to the limit of its absorption coefficient, a coefficient which is remarkably high<sup>1</sup>. Now this excess of food, having been so absorbed and having arrived within the tissues, obviously increases the weight of the body by its own weight, and will ever after continue to be a part of the body's weight until united with oxygen and carried out of the body as  $\text{CO}_2$ ,  $\text{H}_2\text{O}$  and the nitrogenous by-products of protein.

2.—Oxygen is taken into the tissues only as needed moment by moment. The ceaseless demand of the tissues for oxygen cannot be stayed, withheld or substituted. Having once entered the tissues, it never returns to the outside world without bringing along with it its "definite proportion" of carbon and hydrogen, which decrease the weight of the body by their own weight.

3.—The weight of the body, from its one-cell stage to death, is merely its net balance of intake and outgo of atoms; the intake being food and oxygen, the outgo being  $\text{CO}_2$ ,  $\text{H}_2\text{O}$  and the nitrogenous by-products of protein utilization.

4.—The oxygen-food balance of the body is similar to a chemical equation, any food which is in excess of the oxygen causing tissue storage and gain in weight, and any oxygen which is in excess of the food causing tissue destruction and loss in weight.

5.—A multitude of pathologic as well as normal conditions cause disturbances in the oxygen-food balance, some causing an increased, some a decreased utilization of oxygen; some causing an increased, some a decreased demand for food; but whether these disturbances be normal or pathologic,

the explanation of their effect on the nutrition of the body must always be in terms of disturbances of this oxygen-food balance.

6.—The ordinary laboratory method of measuring the basal metabolic rate is a very accurate measure of any disturbance in this oxygen-food balance.

7.—So far as diseases of the endocrine glands are concerned, if an endocrine gland is so diseased as to cause an over- or under-production of its secretion and, in turn, to disturb this oxygen-food balance, such a condition will effect the nutrition of the body; otherwise, it will not.

8.—The diseases of the endocrine glands have no specific or mysterious influence in causing the body to gain or lose weight. Their effect, just as in the case of other causes of gain or loss in weight, is due far more to the change they cause in the total metabolism than to the changes they cause in the basal metabolism.

9.—Diseases of the thyroid, pituitary and adrenal glands cause changes in body weight and are associated with changes in the basal metabolism, as well as with changes in the total metabolism.

10.—Experimental proof of the effect of these glands in causing disturbances in the oxygen-food balance is easily seen if extracts of these glands are injected into the blood stream. The rate of oxygen utilization is notably increased and this increase is in proportion to the amount so injected.

11.—Loss of the ovarian or testicular hormones causes changes in the body weight, and these conditions are often associated with changes in total metabolism but not in the basal metabolism. Extracts of these glands, when injected into the blood stream, do not cause an increase in the oxygen intake.

#### References

1.—Jones, H.: A simple device for measuring basal metabolism, *J.A.M.A.*, 1920, lxxv, 538-539, and *Arch. Int. Med.*, 1921, xxvii, 48.

2.—Atwater, W. O.: Principle of nutrition and nutritive value of food, U. S. Dept. Agriculture, 1901, *Farmer's Bulletin*, No. 142.

3.—Atwater, W. O., Benedict, F. G. and others: Experiments on the metabolism of matter and energy in the human body, 1898-1902. U. S. Dept. Agriculture, *Experimental Station Office Bulletin* No. 136.

# The Endocrines in Psychopathology

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HERE are two ways to handle such a huge topic as the relations between the endocrines and the psyche: Write a large book telling what every one else has found and what the author has observed and come to some dogmatic conclusions; or to write a very brief paper and disguise it in philosophic garb. The latter I threaten to do.

The first question which arises is, which is guilty, the endocrines or the psyche? Men like Cotton, of New Jersey, and Mott, of London, say that the physical is at the bottom of all psychologic ills; Mott stressing the endocrines, while Cotton, being more catholic, blames everything that can be removed surgically. They proceed at the operating table and in the autopsy room, with statistics and specimens to prove they are right.

Then there is another school, not quite so rabid, who insist that a disordered psyche can do almost anything—destroy tissue, cause malfunction and produce any number of bodily ailments. They are labeled as dreamers or fools or knaves, by most of the honored medical fraternity.

My field being psychopathology, I am expected to lean toward the latter point of view. I shall not disappoint you.

To make rash generalizations, no matter how rabid, would serve no purpose. So I remind you that scientists—not dreamers like me, but men whom you all respect as careful workers, such as Pavlow, Crile and Cannon—have given you an inkling of the effect of emotional states on the function of the endocrines. If readers scoff too readily I would suggest having the work of these men as an image before you when you read what follows which, to many of you, may seem, at first glance, quite fantastic.

Let us take the extreme instance first, the endocrinologic findings of Mott, of London. He found in a series of autopsies that the gonads of male and female dementia precox patients showed distinct atrophy and disintegration. I shall not question his findings, for Lewis, working at Saint Elizabeth's Hospital, in Washington, D. C., went a step farther and found that, not only the gonads, but practically every member of the endocrine chain was affected in some degree in precox conditions. While Lewis found more, his point of view as to the cycle was

not in accord with that of Mott, who felt that the physical condition was the underlying cause of the mental disorder. Lewis saw a more complicated picture.

Let us see how we can otherwise attack the subject. Let us not think of dementia precox as a name, a diagnosis or a mere state of mind. Let us see, in a measure, what takes place. Let us always ask the question as to *what actually takes place*.

We are all agreed that the precox patient withdraws from the world of reality and draws into his own world of fantasy—he ceases to live in and among the life he finds himself confronted with. A shorter way of putting it is, "he withdraws from life". Whether the gonads be looked upon as merely a source of rather satisfactory amusement or, from the purely endocrinologic point of view, as a source of internal secretion, we cannot deny that in some remote way they are connected with the processes of reproduction—life.

Now just to prove I am not merely making a play on words let me recapitulate. The urge for life in the precox patient is gone, so the drive for reproducing life is gone and there is no stimulus to the glands, and atrophy and disintegration take place.

To those of my readers who are interested I would suggest reading some of Samuel Butler's books on unconscious memory, "Evolution, Old and New," or any one of his four wonderful books which are so stimulating to a wider contemplation of man's deeper metabolic functions, as related to his behavior and his development.

It might not be amiss to go into the why of the precox retreat. A system of ideals has been established, and when the owner of these ideals comes into contact with reality he cannot reconcile them. Violence is done to the system and an attempt is made to establish them in his own psyche. Fulfilment of certain cravings, at various levels lower than those demanded by society, is sought; then lack of fulfilment brings about a conflict which cannot be met in the ordinary walks of life, and this gives rise to various motor acts we term antisocial. These include castration activities, actual and symbolic. Here I emphasize again the gonadal atrophy, which is merely another form of the castration drive. This takes place in an

effort to prevent the fulfilment of tabooed cravings—tabooed by the person, from a series of social images which, no doubt, have certain biologic foundations.

My more skeptical readers would do well, before passing judgment, to study the pre-cox mechanism from what may, for the moment, seem a futile angle. Do not imagine that I am trying to separate soma from psyche. Any such attempt is anti-biologic. However, we can emphasize what is important *relatively*, and it is well, in this remarkable interplay of gland and body, psyche and function, to evaluate the hierarchy, considering the anthropomorphic gradients with their subjective values.

These remarks would not hold for fish, fowl or the lower mammals, but in them we do not have precox conditions, or the various interplay between endocrines and psyche. I have seen endocrine disorders in animals from nutritional and cellular disorders, and, in the main, the situation has been confused because of our having done so much of our work in this general field. Of course, Kendall used cretins.

To leave our psychotic group, with whatever lesson we may have learned, let us for a moment turn to a few examples (not anomalies), which we may gather from the psychopathologic disorders.

Some time ago there came to my notice a patient who was suffering from a thyroid disturbance. She had all of the typical thyroid stigmata—teeth, eyebrows, tremor, etc. The pulse was skyrocketing around 140-160. This patient came under my care before basal metabolism tests were perfected, as at present. But she had other troubles. These consisted of various problems and conflicts which I shall not go into, but which were carefully studied and straightened out. Her pulse dropped in a comparatively short time to around 90; she gained weight; her tremor lessened; her thyroid condition receded into the background—her conflicts had brought it to the fore. I do not treat thyroid conditions in this fashion; I merely mention the coincidence. Perhaps, when we know more of the interworkings of these situations we will handle them with greater success.

There has been no operative procedure in the foregoing case, but the young lady in question has gone along for five years. She married the young man and now has a family well under way, and no thyroid condition disturbs her. This is not magic—just an example.

Another case—a more recent one—a woman of 40, with two boys, 12 and 15 years old. She had had a depression and this was followed by an anxiety neurosis. One of our city's most able endocrinologists gave her thyroid, 1 grain, three times a day. He knew what he was doing, for he had given her a careful metabolism test. After taking the medicinal "proper amount" of thyroid, she felt like jumping out of windows, her skin, or the nearest convenient object. She came to me for well-marked anxiety, her endocrine unbalance being of secondary consideration. It was thought advisable, after consultation with the physician who was feeding her thyroid, to discontinue the treatment. After careful investigation and psychologic adjustment, her metabolism was reestablished to normal.

We could go into a theoretical consideration of the many cases under my care where menstrual irregularities of various types had become adjusted permanently, after many years of faulty function, simply by a readjustment of the psychic disorders. I might add that these women did not come to me for any such purpose—and they were right. They came on account of the psychic difficulties which were at the base of their disorders. They had no conscious inkling of the relationship of their combined difficulties.

We could discuss in some detail the many cases of sexual impotence which have, for one reason or another, come into my hands for treatment. I might sum them up by saying that an ounce of understanding of the underlying psychic situation is worth more than a barrel of assorted glands.

I might mention in passing, a case of diabetes. The patient was an elderly man who had engaged in various business enterprises. He had been successful. He was hospitalized and put at rest, his diet had been adjusted, and he was made "sugar free". Any break in the regime would bring back his diabetic condition. However, we could bring back the diabetic condition by handing him a telegram or by allowing him to receive a telephone message regarding some phase of his business wherein the issue contained some conflicting situation. This was in the days preceding insulin.

My suggestion is, not that the patient be protected from bad news, but that the problem be worked out so that the patient has a thorough understanding of the relation-

ship of his conflicts and his ailments, and that he be put in a position where he can handle the problems of life without anxiety or any of the accompanying destructive emotional disturbances. This requires much more understanding, on the part of the physician, of the interrelationship of conflict and emotional reaction to disease. The works of Cannon, *et al.*, are not theoretical alone but are actual, factual occurrences.

I trust that, from what has been written, no idea will be gained that I am a nihilist and do not believe in the use of endocrine products for therapeutic uses. However, I do have a suggestion as to the general scheme of dosage. In instances where we can, by metabolic rates, determine the bodily needs, as in the case of the pancreas and thyroid, therapy may proceed along the indicated routes. But even in these measurable instances it might be well to consider the idea I am about to formulate.

In cases of endocrine unbalance, no matter how marked (with certain exceptions, as in determined cretins), a certain adjustment and balance has been made by the

body. This holds especially in relationship to the comparative endocrine chain. This is instance in the thyroid-parathyroid removal in female rats, where the breasts, while stimulated by lactation, serve to compensate the missing endocrines and life is maintained. When the rat stops nursing its young, endocrine imbalance ensues and the animal dies.

So, in varying degrees, compensatory operations take place all along the cycle and, in order not to do violence to the new balance established, it is well to proceed with caution and use, at first, minimal doses, for the shock of readjustment is so great as to do more harm than good. This holds especially in the more obscure cases where one is experimenting, as in trying to stimulate the gonads. Personally, I have never encountered a case of impotence which has been benefited by glandular therapy.

I do not assume that I have converted any one to my point of view. If I have established a doubt about certain preconceived concepts I shall feel well satisfied.

## The Endocrine Factor in Hyperesthetic Rhinitis

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**H**YPERESTHETIC rhinitis is a common disease. It is often undiagnosed, and receives but scant attention from the medical man. The patient is seldom disabled by it. None have ever died from it; and as often as not the patient suffering from it is treated with various nasal ointments, drops, irrigations, and is, all-too-frequently, subjected to repeated nasal operations. These procedures are unavailing, and the patient finds what solace he can in the vagaries of Christian science or some other cult.

In order that there may be no confusion it may be well to define terms explicitly before we proceed any further. It is well to define terms as accurately as possible, even at the risk of repeating what is already well known and clearly understood, in view of the controversial nature of the subject.

The condition known as hyperesthetic rhinitis is also designated as vasomotor rhinitis, hyperplastic rhinitis, hyperplastic

ethmoiditis, and non-seasonal hay-fever. Although the views of various writers differ as to the etiology, there is a well defined tendency discernible in some of them to seek the underlying cause of this condition in the field of endocrinology. I share in this tendency and wish to present a series of cases which seem to show a definite and unmistakable endocrine basis for the clinical picture which they present. Although the evidence is not conclusive and does not warrant a dogmatic assertion of the endocrine nature of hyperesthetic rhinitis, it is sufficient for a working hypothesis, upon the basis of which further investigation may logically proceed.

### Symptoms and Signs

In an article published in 1921<sup>1</sup>, concerning the basal metabolism in hyperesthetic rhinitis, the following clinical description of the condition was given by the writer:

"It occurs most commonly in young females, although it is also observed in older women and in the male. The attacks come on regardless of the season of the

year, without exposure to perfumes, odors or irritating vapors. They usually occur in the morning, after arising, and are characterized by paroxysms of sneezing, which have been referred to as the 'machine gun sneeze'—the patient sneezes from a half-dozen to fifty times in one paroxysm. This is followed by a profuse, thin, watery, serous, irritating discharge from the nose, soiling several handkerchiefs. The conjunctivae become more or less suffused and hyperemic. There may be only one attack. In the severe cases, the attack may be repeated many times during the day. In the milder cases the disease may be only slightly annoying to the patient. In the severe cases it may lead to profound mental depression and be the source of a great deal of worry.

"This mental state of the patient is of interest and is, perhaps, of considerable significance and importance in the study of the condition. These attacks may continue for weeks and then subside; and again, they may last for many years.

"Upon examination of the nose between attacks, we find that it appears practically normal, except for pallor of the mucosa. During the attack and for a variable length of time afterward, the turbinates and the mucous membrane lining the septum are waterlogged; the tissues are pale, soft and swollen; the thin, serous discharge gives them a shiny appearance."

The following table of twenty cases of hyperesthetic rhinitis, which I have treated, exhibits, to a greater or lesser degree, most of the peculiarities noted in the foregoing description:

I first suspected that hyperesthetic rhinitis is an endocrine disturbance when a series of cases, studied routinely, showed that the pulse rate in many of them was slow; that there was a subnormal temperature; a great sensitiveness to cold; brittle finger nails; dry hair; dry skin; and general lack of physical energy. It was then decided to do routine basal metabolic tests on these patients, and the results are shown in the preceding table. It is of special interest that there is a constant low basal metabolic rate. These patients all showed a pale, flabby, swollen nasal mucosa, and usually the clinical characteristics associated with hypothyroid secretion; and nearly all were relieved of their symptoms by ophotherapy. The following history is typical of those listed in the table:

*Case 1.*—The patient is a woman of fifty. She is overweight, soft, flabby, blonde. For the past six years she has suffered from frequent attacks of sneezing (paroxysms of forty or more sneezes) and the discharge of copious amounts of thin, watery secretion from the nose. She underwent a partial, bilateral, middle turbinectomy and ethmoid curettage four years ago.

*Examination, Rhinolaryngologic:* Ears normal. Nose, right: (1) evidence of turbinate operation; (2) mucosa pink, except in region of middle meatus, where it is pale and boggy; (3) clear, thin, watery secretion in nose; (4) no polyps, no pus; (5) septum straight, no spurs, etc.; (6) inferior

Name	Age	Sex	Symptoms	Duration	B.M.R.*		B.M.R.*		Results
					Aver. Temp.	Aver. Pulse	Before Treatment	After Treatment	
V. B.	34	F	Sneezing, discharge	8 mos.	99.2	84	-12	0	Cessation of symptoms
Mrs. E. L. H.	30	F	Sneezing, discharge	2 yrs.	97.6	80	-3	0	Cessation of symptoms
Mrs. C. T. L.	50	F	Sneezing, discharge	4 yrs.	97.6	72	-22	-4	Cessation of symptoms
G. E. M.	30	M	Sneezing, discharge	1 yr.	96.8	56	-20	-3	Slightly improved
Mrs. O. M.	40	F	Sneezing, discharge	2 yrs.	98.2	76	-23	0	Cured
R. N.	41 <sup>1</sup> / <sub>2</sub>	M	Sneezing, discharge	2 yrs.	a	b	c	d	Cured
Miss A. O.	21	F	Sneezing, discharge	3 yrs.	98.6	72	-12	0	Cured
Mrs. F. P.	35	F	Sneezing, discharge	?	98.0	64	-7	+20	Cured
Miss B. J. R.	30	F	Sneezing, discharge	2 yrs.	99.0	84	-7	e	Much improved
Mrs. J. J. R.	30	F	Sneezing, discharge	1 yr.	98.8	96	-9	0	Cured
Mrs. R. P. W.	40	F	Sneezing, discharge	Long time	98.4	60	-11	0	Cured
Mrs. O. B. N.	28	F	Sneezing, discharge	6 mos.	98.8	86	-5	+10	Cessation of symptoms
Mrs. N. S. H.	38	F	Sneezing, discharge	3 yrs.	98.0	70	-12	0	Cessation of symptoms
Dr. R.	40	M	Sneezing, discharge	10 yrs.	f	?	?	?	Symptoms disappeared
Mrs. I. O.	50	F	Sneezing, discharge	3 yrs.	98.6	72	-1	+5	Entirely relieved
Miss M. T.	24	F	Sneezing, discharge	2 yrs.	98.0	68	-18	-3	Entirely relieved
Miss M. F.	19	F	Sneezing, discharge	1 yr.	97.6	78	-3	+2	Cured
†Mrs. R. W.	25	F	Sneezing, discharge	10 mos.	98.4	78	0	0	Symptoms disappeared
J. S.	8	M	Cretinism, hyperesthetic rhinitis	?	?	?	?	?	Myxedematous condition much improved. Hyperesthetic rhinitis cured.
V. A.	6	F	Cretinism, hyperesthetic rhinitis	?	?	?	?	?	Myxedematous condition much improved. Hyperesthetic rhinitis cured.

\* B.M.R., abbreviation for basal metabolic rate.

† The basal metabolism test done on Mrs. R. W. was not done under basal conditions. This was not known to us at the time of the test.

a Subnormal.

b Irregular.

c Not done.

d Not done.

e Variable.

f No record.

NOTE: The treatment of all these cases consisted of the administration of thyroid extract. (Hynson, Westcott & Dunning.)

turbinate, boggy. Left: (1) evidence of turbinate operation; (2) mucose of entire nasal chamber very pale; (3) thin, watery secretion in nose; (4) no polyps, no pus; (5) septum normal but pale; (6) inferior turbinate is hypertrophied. Pharynx normal except for dilated capillaries on post-pharyngeal wall; tonsils atrophied. Larynx, mucosa pale.

*Exam., General:* Pulse average 72; temperature 98.8°F. The temperature is generally subnormal, but during one period of five days, during a "cold," the temperature was brought to normal by a temporary 'pyrexia.

In this case the basal metabolism was low. On certain occasions the rate was as low as minus thirty. Upon the administration of thyroid extract,  $\frac{1}{4}$  grain, three to four times a day, the metabolic rate was increased, and paralleling the increase in the rate of metabolism a subsidence of the symptoms was noted. When the basal metabolism reached normal the symptoms—sneezing, watery discharge and mental depression—disappeared. At this point thyroid medication was stopped.

After the lapse of three or four months the symptoms returned and the basal metabolic rate was again found to be low. Thyroid medication was resumed and the symptoms once more disappeared when the basal metabolism reached a point within normal limits. This required a period of eight to ten days, when the patient was again free from her symptoms. She has been under observation for over two years, and it is necessary to keep her metabolism up by the periodic administration of thyroid extract, in order to keep her free of symptoms.

This case is typical of those summarized in the preceding table, although it shows in a much more striking manner than most of them the dependence of the patient's well-being upon the rate of her basal metabolism. It should be noted in this case, as well as in the others, that there were times during the period of two or three years when the administration of thyroid extract apparently failed to improve the symptoms, but on investigation it was found that the extract had been purchased at a corner drug store, where it had lain on the shelves for a long time and had become inert.

#### Confirmations of Endocrine Basis

In studying the literature to see how far my view, that hyperesthetic rhinitis with a thyroid syndrome is an expression of endocrine disorder, is shared by other observers, it is noted that, in regard to the skin and mucous membrane involvement, Hutinel and Mailett<sup>2</sup>, in treating glandular dystrophies, refer especially to the tegumental changes in myxedema. They note that the

cell elements of the skin are infiltrated by fat and by a substance analogous to mucin; also that the three elements—myxedematous infiltrations, surcharge of fat, and tendency to sclerosis—are the origin of the dermal alteration, especially in glandular dystrophies dominated by thyroid insufficiency.

Berard<sup>3</sup> states that, in myxedematous subjects, at autopsy, the most habitual lesions consist of infiltrations of the tegument and the mucosa by mucin; in thyroid myxedema the cutaneous dystrophy and edema is not accompanied by intellectual deficiency, while in parathyroid myxedema it is.

McCarrison<sup>4</sup>, in the histologic examinations of a section of myxedematous skin, also observed that the skin and mucous membrane were infiltrated by a substance resembling mucin, and that the mucous membrane of the nose was similarly affected. Lortat-Jacob and De Gennes<sup>5</sup> state that in myxedema the endocrine disturbance apparently determines the appearance of skin and mucosal lesions, which resist all treatments except otopharmacy.

Leopold Levi and Rothchild<sup>6</sup> say that patients with hypothyroidism are especially affected by the least disturbance of external temperature (coryza). The mucous membranes are pale, opaque and may be swollen like the skin, which is most obvious in the mouth and nose. The mucosa of the hypothyroid subject is most easily infected and autoinfected.

As regards the basal metabolism, it is well known that the rate is greatly decreased when the thyroid secretion is deficient, as in myxedema, etc. It remains to be shown what clinical or other support there is that hyperesthetic rhinitis is accompanied by a decreased metabolic rate. My own original communication on this subject, published in 1921, has since been supplemented by the observations of others. Selfridge<sup>7</sup> refers to certain cases of disturbed metabolism in respiratory conditions of undoubted endocrine origin. In a previous article, Selfridge<sup>8</sup> mentioned several cases of vasomotor rhinitis, which he considered to have an endocrine basis. He thinks that this condition particularly is related to disturbances in the functions of the autonomic system, and that there is slowly accumulating evidence that the ductless glands play a part in this disturbance.

Lee<sup>9</sup> mentions two cases of vasomotor rhinitis with very low basal metabolism and the usual symptoms of hypothyroidism, both of which markedly improved under thyroid

therapy. Sonnenschein and Pearlman<sup>10</sup>, on the other hand, doubt that lowered metabolism is present in hyperesthetic rhinitis. In four out of five cases observed by Simpson<sup>11</sup>, the basal metabolism was normal; in the fifth case it was below normal and the symptoms ceased on thyroid therapy. Sonnenschein and Pearlman<sup>10</sup> say that it has been definitely shown that a lowered metabolism is not usually present in hyperesthetic rhinitis.

Having referred to the important points of contact between hyperesthetic rhinitis and the hypothyroid syndrome, I wish to add briefly to some other opinions which connect the nasal condition with endocrine dysfunction. Senesey<sup>12</sup>, speaking of the relation of endocrine changes to nasal neuroses, rather connects the symptoms of hyperesthetic rhinitis with pituitary insufficiency. Mithofer<sup>13</sup>, in studying a patient with constant infiltration of the nasal mucosa, found symptoms of mild hypothyroidism, and Beck<sup>14</sup> claims that hyperplastic ethmoiditis is due to hyposecretion or dysharmony of one or more of the ductless glands; and "that the pathologic changes found in the middle turbinates and curetted portions of the ethmoid, in asthma and in non-suppurative sinusitis, are very striking, in that the bone shows rarefaction, somewhat resembling that found in early bone changes of osteomalacia, acromegaly and otosclerosis. This pathologic finding is suggestive of a possible etiologic factor in some disturbance of the glands of internal secretion.

Kauffman<sup>15</sup> also refers to the histologic bone findings in hyperplastic ethmoiditis as being similar to those observed in deficiency diseases, especially insufficiency of fat-soluble vitamine A. Kauffman thinks that the ethmoid bone changes are apparently due to some disturbance in the nutrition of the overlying mucous membrane. Ballenger, in the last edition of his textbook<sup>16</sup>, says that

many of the nonallergic types of vasomotor rhinitis show some endocrine imbalance; faulty metabolism, hypo- and hyper-endocrine functioning may be factors in sympathetic reactions, of which vasomotor rhinitis and allergy are possible related expressions. Maybaum<sup>17</sup> thinks that the continuous irritation of the mucous membrane in hyperplastic ethmoiditis may be due to a protein sensitization, but that endocrine disturbances are not infrequently associated conditions.

### Conclusions

It has not been conclusively proven that hyperesthetic rhinitis is but a symptom of hypothyroidism, although, in my own mind, there is no escape from such a conclusion. A large series of cases studied by various observers will prove or disprove this theory. There may be other factors of significant importance brought out. The question why all hypothyroids do not have hyperesthetic rhinitis must be answered.

### References

- 1.—Novak, F. J., Jr.: *Wisconsin M. J.*, Mar., 1921.
- 2.—Hutinel and Maillet: *Ann. de Méd.*, Paris, 1921, x, 89.
- 3.—Bérard: "Le Corps Thyroïde. (Nouv. Traité de Chir., Paris, 1908)", pp. 29-34.
- 4.—McCarrison: "The Thyroid Gland," 1917, p. 180.
- 5.—Lortat-Jacob and De Gennes: *Bull. et Mem. Soc. Méd. de Hop.*, Paris, 1924, xviii, 794.
- 6.—Leopold-Levi, and Rothschild: *Compt. Rend. Soc. de Biol.*, Paris, 1906, lx, 745.
- 7.—Selfridge, G.: *Laryngoscope*, 1922, xxxii, 243.
- 8.—Selfridge, G.: *Laryngoscope*, 1920, xxx, 611.
- 9.—Lee, R. I.: *Med. Clin. of N. Amer.*, 1925, viii, 1705.
- 10.—Sonnenschein, R. and Pearlman, S. J.: *J.A. M.A.*, 1924, lxxxii, 1973.
- 11.—Simpson, W. L.: *Laryngoscope*, 1922, xxxii, 768.
- 12.—Senesey, E. T.: *Ann. Otol.*, 1925, xxxiv, 183.
- 13.—Mithofer: *Laryngoscope*, 1923, xxxiii, 371.
- 14.—Beck, J. C.: *Laryngoscope*, 1927, xxvii, 425; *Amer. Laryng., Rhinol. and Otol. Transactions*, 1912, p. 71.
- 15.—Kauffman, A. B.: *Laryngoscope*, 1922, xxxii, 54; and *Ann. of Otol., Rhin., and Laryng.*, 1922, xxxi, 582.
- 16.—Ballenger: "Diseases of the Nose, Throat and Ear", 5th Ed., 1925, p. 287.
- 17.—Maybaum: *Am. J. Surg.*, 1922, xxxvi, 177.

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# Relation of the Ductless Glands to Obesity

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HERE are many reasons why the medical profession should interest itself in the serious study of obesity. The periodic health examination extends the doctor's field of usefulness. At the present time there is about one doctor to every 800 of the population, and of that 800 he sees only the acutely ill. Periodic health examinations bring him in contact with the supposedly healthy. It will bring to the doctor's attention many who are overweight and many who are actually obese, and this obesity should be considered seriously.

It is estimated that there are between 500,000 and 1,000,000 diabetics in the United States. Most of these were fat before they became diabetic.

Fat handicaps the individual in his effort to get about and attend to his ordinary vocation—he becomes clumsy and awkward, short of breath, and has a lessened capacity for work; his clothing costs him more, not only as to the original cost but also as to the upkeep; it lessens resistance to infections; if a surgical operation becomes necessary, fat adds to the danger of the anesthetic, increases the mechanical difficulty of the operation, and the likelihood of infection; blood pressure is increased.

Life insurance companies view a fat individual as a poor risk and penalize him by adding to the premium rate. I understand that some companies add five percent to the premium for each inch by which the waistline exceeds the girth of the chest.

Fat slows down the mental processes.

It was Caesar who said that he wished to have about him sleek, well-fed men—they were not dangerous; but he viewed Cassius with some suspicion because he was a lean individual, and Caesar felt that lean men thought too much; i.e., their brains were more active than those of fat men.

It is said that each pound of fat adds 4,500 linear feet of blood vessels to the body. By the time the person is thirty pounds overweight you can see what an enormous burden has been thrown on the heart and kidneys.

Heretofore the public has been much more interested in obesity than has the profession, but there are some indications that the profession is about to take an interest in this important subject.

When the newspapers deal with obesity they usually consider it as if all obesity were of the so-called "exogenous" variety and constantly stress the value of diet in its control, so that all sorts of freak diets are discussed about our tea tables and card tables and practiced by our wives and mothers.

That overeating is a fault, goes without saying. During the War, for example, when the population was on reduced rations, gout, diabetes and obesity almost disappeared from Germany; while during the palmy days of the Roman Empire, when overeating was popular, gout appeared even among the women.

## Classification

The classical division of obesity is into the exogenous and the endogenous varieties. This is probably an erroneous classification. The metabolic defect is probably the same in the two classes, differing in degree only, being much more serious in the so-called "endogenous" type.

Another division is into the anemic and the plethoric types.

The anemic type is the fat, flabby individual, who has little strength or endurance. This variety is probably due to thyroid deficiency and is best exemplified by the person with frank myxedema or high-grade hypothyroidism.

Persons of the plethoric type are active, both mentally and physically. They are strong-willed, make decisions quickly, and have the mental and physical power to carry out their decisions. They have rather more than the average hair suit, exhibit more than average perspiration, and have plenty of strength and endurance.

Strouse and his associates suggested the following classification:

- 1.—*Mast-fettsuch*; due to overeating, underwork, or both.
- 2.—*Thyrogenous*.
- 3.—*Constitutional*; due to neither of the above causes.

There is no constant relation between constitutional obesity and the basal metabolic rate (B.M.R.) This is probably only another way of saying that this type of obesity is not of thyroid origin, but is due to some other endocrine defect.

We have probably taken the B.M.R. much too seriously in this connection. It measures the gaseous exchange of the body and probably records the thyroid function accurately; but the total metabolism of the body is influenced by the pituitary, the adrenals, the gonads, and other tissues and organs whose functions cannot be measured by the gaseous exchange of the body.

That obesity is not always due to over-eating is a matter of simple observation. We all know very fat persons who eat much less than their thin friends or relatives.

#### **Metabolism of Carbohydrates and Fat**

St.rouse and his co-workers demonstrated that the obese derive less energy from fat than do either persons of normal weight or persons underweight. They derive more of their energy from carbohydrates.

Some obese persons, especially those of the pituitary type, sometimes exhibit a craving for sweets much resembling that due to hypoglycemia. At the same time they exhibit a low blood-sugar. Hypopituitarism has for many years been known to be accompanied by a high carbohydrate tolerance. It is probable, in this pituitary type of obesity, that the carbohydrate and fat are stored instead of being burned; i.e., the transportation of these two foodstuffs is so rapid that they get into the liver, muscles, and tissues before the oxidative processes of the body are able to convert them into heat. In diabetes there is a defect in fat metabolism almost as serious as that of carbohydrate metabolism. After a meal, lecithin should increase in the blood stream, but it does not; cholesterol should not increase, but it does; the fat appearing in the blood after a meal should be absorbed by the red blood cells, but it isn't.

We are coming to feel that cholesterol is in some way intimately related to arteriosclerosis and that probably diabetics develop this condition more frequently than do average individuals because their fat metabolism is disordered so that cholesterol increases in the blood stream. The necessity for giving the diabetic patient more than the average amount of fat in his diet tends to aggravate this disorder.

Insulin has a double action in the metabolism of carbohydrates: It enables the body, not only to oxidize these substances, but also to store them as glycogen and fat.

Pituitrin neutralizes the action of insulin, if the two are given at the same time. But if insulin is given first, pituitrin has an

inconstant action in combating its effects; i.e., pituitrin does not have a constant effect in raising the blood-sugar after insulin has reduced it. One might gather from this that pituitrin combats the storage function of insulin, but that after carbohydrates are removed from the blood stream, either by oxidation or storage, pituitrin has comparatively little power to get them out of the liver, muscles, and other warehouses of the body. It may be that pituitrin, not only prevents the too-rapid withdrawal of the carbohydrates for storage, but also increases their oxidation.

Adrenalin (epinephrin) combats the action of insulin in different way. After the blood-sugar has been lowered by insulin, epinephrin promptly raises it by unlocking the warehouses of the body and putting glucose into circulation again.

#### **The Specific, Dynamic Action of Food**

The same kind and quality of food, fed to two different persons, produces two different values of energy. The same thing might happen in the case of two different engines (unless they were very carefully standardized)—one might produce more steam from a ton of coal than the other, depending on the condition of its flues, the regulation of the drafts, and various other factors.

That food has different dynamic values in two different individuals probably indicates only that their metabolic processes are not the same. This is perhaps due to the different total endocrine activities in these persons, and not merely to a difference in their thyroid activity.

#### **Glands Involved**

The thyroid is the one probably most frequently involved. Certainly it is the one whose deficient function is most readily detected. If it be accompanied by hypopituitarism of the posterior lobe, the diagnosis is more difficult, because the basal metabolic rate is apt to be normal or above normal, in spite of considerable degrees of thyroid deficiency. The explanation for this has never been made, so far as I know, and this curious fact is a matter of clinical observation only.

Thyrogenous obesity is accompanied by the usual signs of hypothyroidism, the more prominent of which might be enumerated as follows:

#### *Subjective complaints:*

Loss of strength and endurance—loss of "pep".

Neuritis-like pains, sometimes resembling those of tabes.

Retarded mental processes.

Cold extremities and sensitiveness to cold.

Catarrh of the upper respiratory tract—asthma.

Stiffness of muscles and joints, worse in the morning.

Tinnitus; catarrhal deafness; vertigo.

*Physical findings:*

The skin is dry; in color it is pale, like alabaster, or yellowish, like parchment, with a flush over the malar prominences.

The hair is dry and brittle on head, scant in axillary and pubic regions and frequently missing on the extremities. The outer thirds of the eyebrows are thin.

The nails are brittle, rigid, and contain white spots.

The teeth are of poor quality. If the condition began in infancy, they are irregularly placed.

The bones are slow in developing and the epiphyseal lines are slow in closing. This condition sometimes causes the slow healing of fractures.

*Distribution of fat:*

Padding on the dorsum of the hands and feet, fingers and toes, and in the suprACLAVICULAR SPACES and dorsal cervical area.

Edema of the upper lids, with narrowing of the palpebral fissures.

Thickening of the lips.

Slow pulse; slow respiratory rate; and "minus" basal metabolic rate.

The anemic type of obesity is undoubtedly mostly of thyroid origin.

The thyrogenous type, of Strouse and his co-workers, is, of course, due to hypothyroidism. Figure 1 shows such a universal distribution, and is a good example of the thyrogenous type of obesity.

The pituitary, posterior lobe is frequently involved.

This is characterized by the peculiar distribution of the fat, there being little or none below the elbows or knees or above the clavicles. The fat on the abdomen falls in successive folds, from the ensiform to the pubis, the last fold being a large pad over the mons region. This type also exhibits folds of fat on the lateral and posterior aspects of the thorax (Fig. 2).

The skin is smooth, the hair fine and silky, The nails show no disturbances of metabolism, nor do the teeth. This is in marked distinction to the thyroid type.

The metabolic rate is usually near normal; in other words, the basal metabolic rate is no measure of pituitary function.

Mentally, this type of obese person is quick and bright, making decisions quickly. Physically, they are well-muscled, with a good deal of strength but not much endurance. They are active and energetic, both mentally and physically.

When hungry, they have a peculiar craving for sweets and develop many symptoms of mild hypoglycemia. They become nervous, irritable, weak and depressed. These symptoms are quickly relieved by the use of some readily-assimilable carbohydrate, like sugar or candy. The blood-sugar at such times is quite low. Cushing, many years ago, called attention to the high carbohydrate tolerance of hypopituitarism.

It seems likely that, in the presence of a deficient amount of pituitrin, the carbohydrates are quickly transported to the liver, muscles, and other storehouses of the body



Fig. 1.—Shows a thyrogenous type of universal distribution of obesity. This woman lost seventy pounds in one year. Her shoes were one size narrower at the end of one year's treatment, showing the universal reduction in the obesity. Her general health showed an improvement equal to her loss in weight.

Fig. 2.—This shows the pituitary type. This lady complained of headaches and lack of strength and endurance. Note the folds of fat on the abdomen and the lack of fat above the clavicles. Rapid loss of weight and disappearance of the headaches occurred under a slight reduction in the diet and pituitary medication. Gain in strength and endurance was even more rapid.

and stored as glycogen and fat, with a consequent lowering of the blood-sugar and signs of hypoglycemia. This was probably the theory back of the action of Gordon, of Philadelphia, who recently undertook the reduction of the obesity of a number of nurses. They were allowed a few pieces of candy between meals, when the hunger became extreme; these were to be taken very slowly. It is probable that, in such cases, the blood-sugar was so low that a little carbohydrate introduced at such times could be oxidized without any of it being stored as fat. This serves to relieve some of the most distressing symptoms of the reduction treatment, in that it prevents the hunger to a certain extent and allows the patients some of the food they most desire.

Treatment directed along the lines indicated produces changes in the patient's feelings and weight that tend to corroborate the correctness of these views; *i.e.*, given pituitrin hypodermically and pituitary by mouth, they lose their ravenous appetite for sweets and show a satisfactory loss of weight, with a corresponding improvement in their sense of well-being and a gain in strength and endurance. I usually give pituitrin "O," 0.5 cc., twice a week, and a specially-coated tablet of the whole pituitary, 3 grains, three times a day.

The relation of the adrenal cortex to obesity is less well understood than that of either the thyroid or the pituitary.

Tumors of the cortex are usually accompanied by obesity and by an increase in muscular strength. If the tumor occurs in a female, she usually takes on some male

characteristics — increase in muscular strength; the voice becomes heavy; there is an increase in the hair suit over the body (though usually there is a reduction in the amount of hair on the head, many times amounting to baldness); the skin becomes rough; there is an increase in perspiration; and an increase in blood pressure.

Marine believes that many of the symptoms of exophthalmic goiter are due to deficiency of the adrenal cortex. The patient having exophthalmic goiter usually exhibits exactly the opposite symptoms from the person showing the plethoric type of obesity. The plethoric type of obesity shows considerable muscular strength, an increase in the amount of body hair and a ruddy complexion. These patients are phlegmatic rather than nervous; composed and decided rather than the reverse, as in the case of the exophthalmic goiter patient. The high blood pressure and the arteriosclerosis that frequently accompany this type might easily be attributed to a hyperfunction of the cortex. The relation of the cholesterol metabolism to arteriosclerosis, and of the adrenal cortex to cholesterol metabolism, rather strengthens the idea that hyperfunction of the



Fig. 3

Fig. 4

Fig. 3.—This woman gained 80 pounds in 18 months after the birth of her first and only child. She also developed a typical diabetes insipidus a little later. To this was added renal diabetes—glycosuria with a normal blood-sugar. Reduction in weight was difficult, though her renal diabetes and diabetes insipidus cleared up satisfactorily under pituitary medication. Her subjective complaints of extreme weakness and nervousness also disappeared under this treatment.

Fig. 4.—Same woman as Fig. 3. She discontinued treatment for three years. She now weighs the same as on her first appearance and has diabetes mellitus. She was excreting 360 Grams of sugar in 7000 cc. of urine (5 percent). The hunger, thirst and nervousness disappeared under pituitary therapy alone and the sugar decreased from a little over 5 percent to a trace. The blood-sugar was 252 mgm. when she was passing 5 percent in the urine.

cortex may have a close relation to the plethoric type of obesity. This would also explain the difficulty in obtaining a reduction in this type.

We have no endocrine remedy for a hyperfunctioning gland. While some glands are undoubtedly antagonistic to some others, the antagonism is not strong enough to reduce the hyperfunctioning one to normal

function. The further observation that this type of obese person usually craves fat rather than sweets strengthens the view that the overactive cortex has some rather close relation to this type of obesity.

The gonads also have some relation to obesity. Note the gain in weight occurring at puberty, during pregnancy and after the menopause. Also, many obese women exhibit menstrual irregularities, the periods becoming more scant and the intervals between periods becoming longer. One mark of gonad obesity is the deposit of fat pads in the trochanteric region. Figure 5 illustrates this type.

Gonadal obesity is usually accompanied by thyroid or pituitary deficiency. The decision as to which gland is involved is usually made by a study of the distribution of the fat and a determination of the basal metabolic rate. In the presence of hypothyroidism, the usual signs and symptoms of that condition may be easily elicited.

One measure of the degree of pituitary deficiency is the amount of pituitrin necessary to cause abdominal cramps.

#### General Principles

Any treatment for obesity should have as its first object the improvement in the patient's general health. No treatment should be contemplated that does not have this in view and show a trend in that direction. It is perfectly permissible to undertake the reduction of a patient for cosmetic purposes, if his health is kept in mind and nothing done that would jeopardize this in any way.

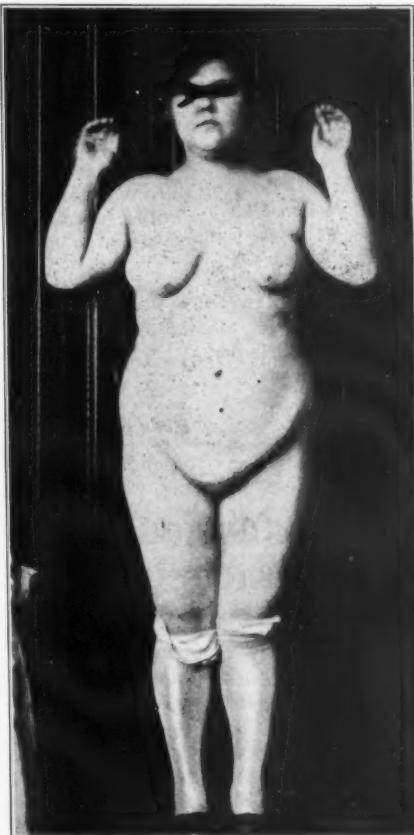


Fig. 5.—An example of probable adrenal cortex and gonadal obesity. This girl was 25 years of age, weighed 252 pounds and had no menstrual period for seven years when she first came under observation. The abdomen was covered with coarse, scraggly hair and there was considerable hair on the upper lip and the chin. The temperature was slightly above normal; the blood pressure was 160/100; the voice was rather heavy; and the muscular development was quite marked. Under the influence of pituitary and ovarian therapy, her menstrual periods were restored, but there was very little reduction in the obesity.

The idea that obesity is entirely a matter of diet—an excess of caloric intake over energy output—should be firmly and finally put out of one's mind, if one expects any degree of success in the majority of cases. That the diet should be reduced and carefully balanced goes without saying; but no patient will stay on a starvation diet indefinitely.

Careful attention should be paid to the condition of the kidneys, heart, lungs, and general body metabolism. Especial attention should be given to the blood, to be sure that a secondary anemia does not develop in cases that are obstinate of reduction.

One should firmly impress the fact on the patient at the outset that obesity is a chronic disorder and that results in the form of weight loss are not to be expected too quickly, and that if this were possible of attainment it should not be attempted.

#### Treatment

Treatment should proceed along several lines:

*First*, one should make the most careful and extensive examination of the patient possible, to be sure that no disorder exists that would contraindicate any of the treatment contemplated.

*Second*, one should determine as accurately as possible the etiology of the obesity, (whether it is the rather rare form of excessive caloric intake, or the more common form of endocrine disorder—pituitary, thyroid, gonad, suprarenal, or a combination of one or more of these).

The diet should be carefully revised. In most cases the easy and correct procedure

is to have the patient keep a notebook, much as Joslin recommends for his diabetics. From this record one can easily change the diet so as to make a considerable reduction in the caloric intake, without seeming to be denying the patient very much. I usually begin by reducing the fats almost to the vanishing point and by eliminating the most concentrated carbohydrates, like potatoes, pastry, candy, and white bread.

*Third*, proceed with whatever endocrine therapy is indicated. This is probably the most important single procedure in the treatment. Thyroid should be given to tolerance and the patient should be carefully watched for signs of overdosage. Pituitrin "O" should be given, 0.5 cc., hypodermically, once or twice a week. The dose may be increased or decreased as the patient's reaction indicates. Gonadal obesity in women should be treated by the use of ovarian residue, 5 grains, three times a day, by mouth, and ovarian residue, 1 ampule, hypodermically, one or more times a week.

*Fourth*, look carefully after the emunctories.

It is sometimes advisable to cut down the intake of salt, and I sometimes use salyrgan or novasurol to expedite the excretion of water.

#### Summary

Most cases of obesity probably have an endocrine basis. This should be carefully sought out and appropriately treated.

The diet should be carefully planned to eliminate most of the fat and the most concentrated carbohydrate foods; the diet should just supply the caloric needs of the patient.

Careful attention should be paid to the general health, to be sure that the measures directed against the obesity are not harmful to the general body economy—"Let us first do no harm."

#### Bibliography

- 1.—Strouse, Solomon: Studies on the Metabolism of Obesity. *Archiv. Int. Med.* 34:367, 1924.
- 2.—Wang, C. C. and Strouse, Solomon: The Metabolism of Obesity. *Archiv. Int. Med.* 36:397, 1926.
- 3.—Gordon, Burgess and Von Stanley, E.: The Use of Dextrose in the Treatment of Obesity: with Special Reference to the Reduction of the Body Weight Without Markedly Lowering the Daily Caloric Intake. *Am. Journ. Med. Sc.* 175:37, 1928.

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## Functional Hypertension and the Value of Certain Liver Extracts in Its Management

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ONE of the problems of present-day medicine is the alarming increase of constitutional diseases and disorders of metabolism. The far greater frequency of cardiovascular affections in recent years has given rise to alarm, and conscientious attempts are being made to educate the people, convincing them of the necessity of adjusting their habits of personal hygiene and teaching them to ease the strain incident to the intense rush of the times. Especially are moderation in eating and regularity in elimination insisted upon.

The seriousness of the problem is shown especially by the frequency of cardiovascular diseases, among the symptoms of which an excessive arterial tension is possibly the most spectacular. This is due partly to the fact that the public have seized upon this factor and the popular diagnosis, "high blood pressure," is a bugbear, as tuberculosis was but a generation ago. While it is true that high blood pressure is a symptom

that may denote several different underlying conditions, the demand is insistent for means to moderate it. It cannot be expected that laymen should differentiate intelligently between the high blood pressure that is a necessary and, indeed, compensatory accompaniment of arteriosclerosis, and the high blood pressure that develops in response to the poisoning of the organism by products of incomplete metabolism. The former is organic and cannot be depressed forcibly without risk; the latter is functional and, therefore, is curable if proper attention is paid to correct nutrition and complete elimination, it being understood that assimilation must be made perfect so that the absorption of incomplete products of metabolism and their unfavorable irritating action upon the circulatory organs may be prevented.

This functional high blood pressure has been designated by the late Clifford Allbutt as *hyperpiesis*, and has formed the subject

of careful study for some years. Its occurrence has been attributed to irregularities in one or several of the endocrine functions; indeed, the majority of clinicians are of this opinion. Crile<sup>1</sup> correlates high blood pressure with hyperactivity of the thyroid gland and believes that this association is sufficiently well established to justify lessening the thyroid activity by excising the gland in certain cases of high blood pressure and myocarditis, in which the only evidence of thyroid involvement, aside from these two symptoms, is the presence of a goiter.

Arne Faber<sup>2</sup> considers the increase of the blood pressure in women to be the first climacteric symptom, and he is supported in this view by many authors. L. Fraenkel<sup>3</sup> looks upon climacteric hypertension as a result of the activity of other endocrine glands that are no longer checked by the ovarian secretion because of the involution of the ovaries. He claims that normally the ovary regulates, checks, or neutralizes these other endocrine actions. Marañon<sup>4</sup> found that, of 106 women who sought medical advice for disorders related to the menopause, more than half presented a more or less marked elevation of the systolic tension. The rise in diastolic pressure was marked to the extent of being in evidence in a group of cases in which the systolic pressure was moderately increased or even normal.

H. Lyons Hunt<sup>5</sup> mentions the case of a maiden lady, age 74, in whom ovarian gonadal tissue was transplanted November 11, 1924. At the time of transplantation, her blood pressure was 220, and on November 18, 1924, seven days after the transplantation, the blood pressure was down to 160. In another case, a widow, age 60, the blood pressure was 240. Ovarian gonadal tissue was transplanted on April 28, 1924. On May 14, 1924, a little over two weeks after the transplantation, the blood pressure dropped to 170, where it remained for a period of six months and then started to rise again, probably due to the fact that the transplanted tissue was beginning to become absorbed. This explanation of climacteric hypertension finds support in Jacob Gutman's<sup>6</sup> observations that the phenomenon is due to pituitary excess. The pituitary excess would naturally be permitted since the ovarian restraint is no longer exercised.

The endocrine nature of functional (or "essential") hypertension is denied by Frederick M. Allen<sup>7</sup>, who says that "endo-

crine disorders are a fad nowadays and they are invoked by some writers to account for practically every obscure condition. Thus they are dragged into the question of hypertension, merely because the pathology is uncertain. But there is no evidence of adrenal excess as the basis of any typical case of hypertension. Thyroid excess may presumably, like any intoxication, aggravate an existing tendency to hypertension, but its status is that of a complication; in typical hypertension there is no hyperthyroidism. The same is true of diabetes and hypertension; they may complicate and aggravate each other, but they are separate diseases, and observations of the frequency of hyperglycemia in hypertension cases and of hypertension in diabetic cases show merely the incidence of these complications. The sex glands have no scientific place in this subject. Castration in either sex does not raise blood pressure. Hypertension develops about the fifth decade of life as frequently in men as in women. A cure of hypertension by ovarian or any other kind of hormonal therapy has not been shown. The so-called hypertension of the menopause responds to diet treatment in the same way as other forms of hypertension. For these reasons the existence of any such separate entity as hypertension of the menopause must be denied."

A. R. Elliott<sup>8</sup> seems to be "on the fence" and, strangely enough, says, "The endocrine glands are regarded by most authorities as having little to do with hypertension." But he points out that after the menopause women show a tendency to increased pressure and that there are more elderly women than men who have abnormally high blood pressure. Our earlier studies lead us to conclude that most authors believe the endocrine glands to be of great importance in the production of essential hypertension. Elliott himself offers "as good a surmise as any other that essential arterial hypertension is, in its inception, a vascular neurosis" in which the hereditary factor is important.

We may add the opinion of Wilber E. Post and Edward J. Stieglitz<sup>9</sup>, according to whom "a metabolic disorder, associated with endocrine dysfunctions of various types and a diminished blood-calcium content, is responsible for many cases of hypertension."

#### Causation

Elliott's surmise; i.e., that essential hypertension is, in its inception, a vascular neurosis, is supported by E. H. Starling<sup>10</sup> who

states that the causation of hyperpiesia must first be sought in the vasomotor centers. Numerous lesions, both vascular and cellular, might reduce the blood supply to this particularly sensitive region and so bring about a compensatory rise in systolic blood pressure.

Functional hypertension is commonly designated as a hypertension in which no organic structural changes have taken place, but this differentiation is difficult to maintain because the two types, functional and organic hypertension, may merge, the first into the second, almost insensibly. Indeed, they are not essentially different, their difference being one of degree only. This view is supported by Lewellys F. Barker" according to whom "high blood pressure appears to depend chiefly on a narrowing of the lumina of the arterioles in the pre-capillary areas. It is at first functional and caused by hypertonus of the arterial musculature, though later it assumes a partly organic character. The different types of chronic arterial hypertension probably represent different stages in the development of the same fundamental process, which may advance with variable rapidity and with variable associated involvements of cardiovascular, renal, cerebral, and other structures in different cases. When recognized early, the process may often be arrested or so delayed in its progress that patients may live comfortably for many years before troublesome symptoms or dangerous complications occur."

The reason why such a vasomotor neurosis or a narrowing of the arteriolar lumina takes place is probably toxemia, or, as Leonard Williams" declares, lowered metabolism. This, he believes, appears to be the explanation of the sustained high blood pressure of advancing years. Just as it is a mistake to suppose that an increase in weight is normal as age progresses, so, in his opinion, it is a grave error to regard high blood pressure as a physiologic accompaniment of the later decades. The latter is just as abnormal as the former, and even more to be dreaded.

Arthur M. Fishberg" includes in the concept of essential hypertension those cases of chronic hypertension that neither clinically nor anatomically can be demonstrated to have evolved from antecedent inflammatory disease of the kidney or from urinary obstruction. However, because of certain exceptional autopsy findings, "essential hypertension cannot be unequivocally defined by the absence of clinical evidence of

nephritis or of urinary obstruction, and it is necessary to add the word 'anatomically' to the definition to prevent the inclusion of those cases of nephritis in which the identity is first revealed at the post-mortem table. This definition is very seriously defective in that it defines the disease solely by exclusion, but, in our present ignorance of the causes of hypertension in general, it does not seem feasible to define essential hypertension in any more satisfactory way. Nevertheless, the consideration of essential hypertension as a distinct nosologic entity seems fully justified, both from a clinical and . . . from an anatomic point of view."

An interesting communication on the relationship of arteriosclerosis and hypertension is presented by O'Hare and Walker", who investigated first a series of fifty cases of arteriosclerosis of the radial, brachial, or temporal arteries, with systolic blood pressure under 145, and found that in this group there was practically no evidence of arteriosclerosis affecting the retinal vessels. In a subsequent group of fifty patients with arteriosclerosis and a systolic pressure over 145, all but one showed a definite amount of sclerosis of the retinal vessels. The groups may be contrasted by stating that, in the hypertensive group, 80 percent had moderate or marked sclerosis of the retinal vessels; whereas, in the non-hypertensive group, 82 percent had either normal retinal arteries or questionable sclerosis. A further group of sixteen patients with normal or low pressure, but who were known previously to have had high blood pressure, presented positive evidence of sclerosis of the retinal vessels. They believe that there is a very definite connection between sclerosis of the small vessels of retinal size and hypertension, but no definite relationship between the peripheral arteries (such as the brachial) and hypertension.

In view of the fact that persistent essential hypertension may lead to arteriosclerosis and to organic hypertension, it is important to discover this condition as early as possible. The differential diagnosis may be quite difficult, and no case can be designated as one of essential hypertension until every possible pathologic factor has been excluded. For this reason, hidden infections of the tonsils, teeth, sinuses, appendix, gall-bladder, colon, uterus, adnexa, and rectum must be sought for persistently and disclosed if present. Also, such other causes as syphilis, aneurysm, sclerosis, saturnism, and

similar general states causative of high tension must be excluded.

Essential hypertension in multiparous, middle-aged, pituitotrophic women (Gutman believes) is due to an increase in blood-pressure-raising pituitary hormone, produced by a greatly hypertrophied, hyperfunctionating hypophysis. The pituitary hormone is a normal factor in the maintenance of arterial hypertension, through its effect upon the cardiac and arterial musculature, and renal and peripheral vessels. The term essential, in this type of cases, is inappropriate and inadequate, and should be superseded by the term *hypertension-dyspituitaria*, which is more rational and scientific and is based upon physiologic data. Hypertension of pituitary origin constitutes no contraindication to surgical interference whenever this is required.

If we now look into the causes that produce an irritation of the vasomotor system, we find that a family history of heart, kidney, or cerebral disease is almost twice as common in a patient with hypertension as in those without increased pressure. Alvarez and Cummings<sup>15</sup> have published the results of their blood pressure studies in several thousand students, and their conclusions as to the importance of earlier warning of vasomotor weakness have been confirmed by other investigators. Such symptoms may indicate a hypertensive diathesis, and, with a susceptible person, steps may be taken to protect against the excessive stress and strain of life.

#### Liver Extracts

Hypertension of the functional or toxic type is usually the result of the presence in the circulating blood of protein split-products; namely, the toxic guanidine bases, cyanamide, the carbamides, etc. Owing to the inability of the liver to carry out its detoxicating function, which is one of several depending on hormone influence, these toxic protein split-products are left to upset the pressor regulation, with the result that various endocrine functions are disturbed. It must be remembered that the detoxicating power through which injurious protein derivatives are built up into urea (which then is eliminated by the kidneys) is a very important part of the work of the liver; and this explains the incidental observation of Macdonald that a liver extract prepared by him caused an existing hypertension to be reduced. Macdonald's results were verified by Major, also by

Harrower and others, who have produced active, hypotensive liver extracts.

This detoxicating and, therefore, in a sense, hypotensive function of the liver, added to the various hepatic functions with which we have been familiar (including the hemopoietin, which is probably responsible for the benefits derived from liver feeding in pernicious anemia) shows the essential and vital character of this largest gland of the body. It well illustrates the physiologic provisions existing in the animal organism for balancing opposing forces and maintaining a suitable equilibrium.

The fact that the liver produces at least one, probably several, internal secretions, was postulated many years ago, especially by French authors, although it was generally denied until recently. Howell<sup>16</sup>, however, in the 1918 edition of his "Text-Book of Physiology," considered the production of glycogen and urea to be manifestations of hormonic action. The discovery of the hypotensive and the hemopoietic principles established the truth of the claim definitely.

These two liver fractions have been isolated by Edwin J. Cohn<sup>17</sup> and his associates. It was found that the fraction responsible for the hypotensive effect is alcohol-soluble; and the other, which is of benefit in pernicious anemia, is alcohol-insoluble but water-soluble.

#### Management of Functional Hypertension

The presence of toxic protein split-products in the circulation is commonly a consequence of intestinal intoxication, together with constipation and intestinal stasis, which themselves may in part be a result of an insufficient hepatic external secretion, namely, bile. The intestinal stasis may be caused partly by the inability of the digestive tract to deal with the substances that have been introduced, and it can be alleviated if foodstuffs that are difficult of digestion and assimilation are eliminated from the dietary. At any rate, some of the most important and quite essential therapeutic measures in the treatment of hypertension resulting from unsatisfactory digestion and assimilation are: First, the rigid restriction of diet in accordance with the patient's ability to take care of it; second, the careful and complete cleaning out and keeping clean of the entire digestive tract. The colon especially must not be permitted to contain food remnants that are subject to fermentation and putrefaction, the products of which, if

absorbed into the circulation, introduce injurious factors and cause disease.

In many cases of functional hypertension, especially when this has not existed for long periods of time, a suitably arranged dietary and adequate removal of all waste products (that is, of undigested and indigestible food) are sufficient to bring about a lowering of the tension. Frequently, however, the endocrine functioning of the liver, as well as its external secretion, has become gravely impaired and may require support.

It is in such cases that hepatic extract is found to be of service, in that it promotes the detoxicating function of the liver and thereby brings about a lowering of an unduly high arterial tension. This seeming depressor effect of hepatic extract, emphasized by Macdonald<sup>1</sup>, was originally considered as a characteristic action of the hepatic solution. Since, as a matter of fact, the effect is brought about through the intermediation of an improved hepatic detoxicating action, hepatic extract cannot be considered strictly as a depressor in the same sense as are the nitrates and similar drugs. Inasmuch as it brings about the desired depression of hypertension through promoting the physiologic corrective processes, it is a regulator—a physiologic remedy and not a pharmacodynamic drug. Indeed, it has been found of service in correcting *hypo-tension* when this was due to intoxication.

#### General Management

When a toxic or functional hypertension has been recognized and the presence of sclerotic changes can be eliminated, the important task confronting the physician is manifestly to prevent the development of such sclerotic changes, which will follow inevitably unless care be taken to eliminate those factors that tend to maintain toxic irritation. Such a result cannot be attained merely by the administration of a depressor drug or a hypotensive animal extract (for instance, liver extract.) The latter is far more promising in its effects because it does not bring about a mechanical depression of hypertension but a detoxication of the circulating blood, whereby irritating substances are eliminated. However, it is first of all essential that no new toxic irritants be introduced into the circulation, and for this reason the source of their supply must be removed. The hypertensive patient must be subjected to a carefully worked out and conscientiously observed regimen, in which his diet, his occupation, indeed his entire mode

of life, are rigidly supervised. In other words, one can hardly speak of a treatment of hypertension; it should be, rather, the management of the patient with hypertension.

One of the most important factors in this management is rest, which, coupled with a suitably restricted diet, frequently suffices to reduce an unduly high blood pressure. When that is the case, the addition of liver extract to the treatment is hardly called for. The hypertension, when once reduced, will not recur unless dietetic errors, excessive strain (physical, mental or emotional), or other causes that upset vasomotor regulation become active again.

In addition to rest and carefully regulated diet, adequate elimination must be insisted upon; and every effort must be made, not only to overcome constipation and intestinal stasis, but to restore lastingly a normal intestinal cleanliness.

The employment of hepatic extract as an additional factor in the management of essential hypertension is of great service in virtually all cases of high blood pressure. However, a notable reduction can be expected only in those instances in which any degree of sclerotic change in the arterial system has not as yet made its appearance. In that event, the administration of hepatic extract will usually result in a notable reduction of both the systolic and the diastolic pressure, amounting sometimes to as much as 60 mm. and more for the systolic

When arteriosclerosis is present, the blood pressure will not be reduced greatly, but a favorable effect on the patient's well-being will be observed, which can be explained readily by the improved detoxication of the tissue fluids. It should be remembered that the proper management of arterial hypertension attempts to remove the cause of the trouble; that it is not the hypertension that is treated but rather the liver, which has failed in its regulating function. When the toxins are removed and the irritation produced by them is eliminated, the effect of this irritation upon the vasomotor system will naturally disappear. It is in this way that high blood pressure is corrected, and it will remain corrected so long as no further toxins of intestinal origin enter the circulation.

For the purpose of presenting some clinical evidence in support of the usefulness of hepatic extract, we may cite a communication by Maurice F. Lautman<sup>2</sup>, who studied

thirty-four patients with hypertension, twenty-six of whom were over the age of forty-eight. Eleven were women and twenty-three were men. These patients received a hepatic extract that had been obtained by subjecting a mash of fresh calves' liver to prolonged extraction with 80 percent alcohol. The filtrate was allowed to evaporate slowly. When the alcohol concentration reached from 90 to 95 percent, the precipitate was collected and dissolved in distilled water. The amount of extract that neutralized the pressor substance contained in 1 cc. of a 1:1000 epinephrin solution was used as the unit of dosage.

Under this treatment, gradual reductions in the systolic pressure, ranging from 30 to 100 mm., with corresponding lowering of the diastolic pressure, were noted following courses of treatment varying from ten to twenty-four daily injections. In two cases with pronounced arteriosclerosis, no lowering of the blood pressure could be affected.

Patients under treatment were quick to notice the improvement in their feeling of well-being, the symptoms referable to the hypertension being rather promptly relieved. Vertigo, present in six cases, was benefited. Headaches (six cases), palpitation (four cases), intermittent claudication (one case), and anginoid pains (two cases) were improved. In five cases with evidences of rather marked renal involvement, there was noted a decrease in the albuminuria following the treatment. No untoward reactions or results, either during or after the treatment, were noted, although over seven hundred injections were given. All the treatments were given hypodermically.

Doctor Lautman offers the following conclusions:

"1.—Extract of liver contains a principle which is capable of reducing the blood pressure

"2.—It exerts a favorable influence on the symptoms which result from increased blood pressure.

"3.—In thirty-four cases studied, there was a gradual lowering of the systolic blood pressure of from 30 to 100 mm. of mercury. Only two cases failed to respond to the treatment.

"4.—No untoward reactions or results were noted from its use."

A physician in the Northwest, a friend of the present writer, who does not wish his name used, reports that hepatic extract is just as wonderful as insulin. His experience has been almost 100 percent satisfactory.

#### Case Reports

*Case 1:* A woman, age 58, blood pressure 300, confined to bed, blind, and ready to die. All resources were exhausted. Hepatic extract, given orally (five tablets a day), reduced her blood pressure to 210, but it then went up to 225. When the dosage was reduced to one tablet, t.i.d., the pressure rose to 240. So long as five tablets a day are taken, the tension remains at 225. Sight is almost normal; there are no more headaches or dizziness, and the patient is up and doing her housework.

*Case 2:* A woman, with a blood pressure of 200/85; fulness in head, insomnia, neck stiff, throbbing in the head and ears, dizzy, sight hazy, arms and hands "sleepy," dyspnea on exertion, palpitation of the heart. All tests were negative, and there was no response to ordinary treatment. The blood pressure on March 5, 1928, was 200/85.

Hepatic extract, one tablet t.i.d., was prescribed. On March 12, the pressure was 185/90, the symptoms were disappearing and the patient felt better. On March 19, the blood pressure was 178/85 and there was a feeling of weakness. On one tablet a day the tension remains at 185/90. Now she feels well in every way and all symptoms are gone. The doctor intends to try one tablet b.i.d., to reduce the pressure gradually.

In small series of cases that were treated under the present writer's observation, eight were listed as arteriosclerosis or nephrosclerosis, and, in these, an average reduction of 33.25 mm. in the systolic pressure and of 11.5 mm. in the diastolic was observed. In this group, the highest systolic pressure recorded was 250, and the lowest 146.

Of fifteen cases diagnosed as functional hypertension, the highest systolic reading was 224 and the lowest 140. Treatment with hepatic extract brought about an average reduction of 33.9 mm. systolic and 11.8 mm. diastolic. In four cases in which no differential diagnosis was made, an average reduction of 81 systolic and 24 diastolic was observed.

Miller and Martinez<sup>2</sup> found liver extract to be of service in the hypertension induced by toxemia of pregnancy, and incidentally the toxemia was greatly improved. These authors are convinced that liver extract has a detoxicating effect in the toxemias of pregnancy and they present a report on a series of cases—seven of eclampsia and forty-three of preeclamptic toxemia. Liver extract was the only drug used in the treatment. The diet and activities were not restricted, except in those patients who showed a blood pressure over 180 mm. The dose varied with the individual. In the

active eclampsia the extract was given intravenously, often in doses of 20 cc. every 15 or 30 minutes, depending on the drop in blood pressure and the state of coma. In the other cases, the pressure was kept down by the injections, given daily for a few days, then semi-weekly, and ultimately weekly.

The rapid abatement of the symptoms is noteworthy: Headaches, dizziness, spots before the eyes, epigastric pain, rapid pulse, nervousness, and coma disappeared in the course of a few hours. The edema of the extremities and of the face disappeared in a few days and did not return so long as adequate dosage was given. The urinary output increased, the albumin decreased and in some cases disappeared entirely. Casts usually disappeared before the albumin. The blood chemistry gradually improved.

M. J. Flipse<sup>1</sup> reported on six unselected cases of advanced hypertension in which liver extract was used for a considerable length of time. He found that the liver extract reduced the blood pressure in patients with kidney disease, but its effect was not usually permanent. However, the general well-being of the patient is usually improved by the continuous administration of liver extract, which is an adjunct in the treatment of hypertension and of special value where the pressure is at dangerous levels. In many cases in which nitrates and related vasodilators failed to reduce the blood pressure, Dr. Flipse found the liver extract effective.

The present writer has treated, and is still observing, a number of patients with toxic hypertension, all of whom have responded well to a regimen in which liver extract was an important factor, although

rest, restricted diet, and effective elimination were insisted upon. He has been in touch with numerous physicians whose observations agree with his own. The interesting part is that favorable results are by no means restricted to patients with only toxic hypertension but that patients with arteriosclerosis are benefited by this treatment, even though a notable reduction of the blood pressure may not be obtained.

#### Bibliography

- 1.—Crile, George W.: *Am. Med.*, June, 1923, xviii, pp. 398-391.
- 2.—Faber, Arne: *Acta Medica Scandinavica*, 1924, Ixi, p. 53.
- 3.—Fraenkel, L.: *Deutsch. med. Wochenschr.*, July 25, 1924, I, p. 1007.
- 4.—Marañon, G.: *Rev. franc. d'endocrinol.*, Dec. 1924, II, p. 408.
- 5.—Hunt, H. Lyons: *Med. Times*, April, 1927, Iv, p. 75.
- 6.—Gutman, Jacob: *New York Med. Jour.*, July 6, 1921, cxiv, p. 31.
- 7.—Allen, Frederick M.: *New York State Jour. Med.*, May, 1925, xxv, p. 726.
- 8.—Elliott, A. R.: *Am. Jour. Med. Sc.*, Aug., 1927, clxxiv, p. 224; reported *Can. Med. Assoc. Jour.*, Jan., 1928, xviii, p. 97.
- 9.—Post, Wm. E., and Stieglitz, Edward J.: *Am. Jour. Med. Sc.*, May, 1926, cxxii, p. 648.
- 10.—Starling, E. H.: *Brit. Med. Jour.*, Dec. 19, 1925, II, p. 1163.
- 11.—Barker, L. F.: *Tr. Ohio State Med. Assn.; Jour. Am. Med. Assn.*, July 24, 1920, p. 269; *Ohio State Med. Jour.*, Oct., 1920, xvi, p. 709.
- 12.—Williams, Leonard: "Middle Age and Old Age." Oxford University Press, 1925, p. 159.
- 13.—Fishberg, Arthur M.: *Arch. Int. Med.*, May, 1925, xxxv, p. 650.
- 14.—O'Hare, J. P., and Walker, W. G.: *Arch. Int. Med.*, March, 1924, xxxii, p. 343.
- 15.—Alvarez, W., et al.: *Arch. Int. Med.*, July, 1923, xxxii, pp. 17-30.
- 16.—Howell, Wm. H.: "A Textbook of Physiology." W. B. Saunders, Philadelphia, 1918, p. 829.
- 17.—Cohn, Edwin J., et al.: *Jour. Biol. Chem.*, July, 1927, lxxiv, No. 1.
- 18.—MacDonald, W. J.: *Proc. Soc. Exper. Biol. and Med.*, 1925, xxii, p. 483; also *Can. Med. Assoc. Jour.*, July, 1925, xv, p. 697.
- 19.—Lautman, Maurice, F.: *Med. Jour. and Rec.*, June 2, 1926, cxxii, p. 751.
- 20.—Miller, Harold A., and Martinez, D. B.: *Am. Jour. Obstet. and Gynec.*, Aug., 1927, liv, pp. 165-175.
- 21.—Flipse, M. Jay: *Jour. Florida Med. Assn.*, Oct., 1927, xiv, p. 185.

## Psychoendocrine Aspects of Dementia Precox\*

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IN 1926, Gabriel Langfeldt completed a remarkable series of investigations upon the cases of dementia precox of the catatonic and hebephrenic type in the hospital at Bergen, Norway. His object was to determine whether or not there is any relationship between these conditions and the endocrine disturbances found so frequently to accompany them.

"In modern psychiatric literature we frequently come across the hypothesis that dementia precox is an endocrine complaint," says Langfeldt<sup>1</sup>. "Only a few of the works on the subject are, however, accompanied by real and exact researches that might give rise to such hypothesis." The reason for this persistent suspicion that there is an endocrine genesis in these cases is because of the "comparatively frequent origin of the complaint at puberty, its relation to the

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menses, Abderhalden's reaction, and similar symptoms." More recently, however, there has been additional evidence available, thanks to perfected laboratory methods, such as the studies of the basal metabolism, the glucose tolerance, etc.

The conception of dementia precox as an endocrine-produced syndrome—an autointoxication emanating from the sex glands—seems to have been conceived and championed by Kraepelin<sup>7</sup> in the nineties. As a basis of this hypothesis, he noted the outbreak of the disease at the age of puberty, the several anomalies in the patient's sex functions, and the many relations of the disease to the processes of generation. He had also noted the frequency of enlargement of the thyroid, brady- and tachycardia and changes in the skin somewhat similar to those seen in myxedema. He had observed abnormalities in the size of the pupils, in acute cases, as well as tremor and exophthalmos.

#### Dementia Precox an Intoxication

At one time Kraepelin favored the hypothesis of an autointoxication from the sex glands, but later leaned rather toward the idea of general metabolism intoxication. Fauser<sup>8</sup>, however, observing that "catabolic ferments for the sex-gland albumin are frequently met with in the blood of dementia precox cases," made use of Abderhalden's dialyzing method, which is based on the fact that the ordinary albumin molecules do not dialyze through animal membranes or parchment. When proteolytic ferments are present, however, the albumin molecules will split up when absorbing water, thereby forming peptones that are capable of permeating these membranes. Thus, by testing the albumin from the various endocrine glands it is possible to find out for which of these there are catabolic ferments in the serum concerned.

As reported by Langfeldt, Fauser carried out Abderhalden's reaction in blood from 250 cases of insanity, and found in dementia precox—in contrast to his results in other psychoses—a destruction of the albumin from the sex glands, as well as from the cerebral cortex, and also the thyroid gland, in a predominant number of cases, but not from other glands. Serum from females only contained catabolic ferments for the ovaries; and serum from males, only ferments for the testes. In quiescent cases, where the process had come to rest, he found no ferments either for the sex glands or for the cerebral cortex.

Fauser's interpretation of this is, "that there must be a dysfunction of the sex glands as well as the cerebral cortex in dementia precox, and, as the destruction of the sex gland albumin is most prominent in acute cases, he supposes the primary seat to be in the sex glands (on congenital basis), with a secondary toxic destruction of the brain."

There are several other observers who agree with Fauser. But Ewald<sup>9</sup>, although always finding a positive reaction in catatonic and hebephrenic cases, obtained negative results in the paranoid and the so-called schizoid cases. Kafka<sup>10</sup>, on the other hand, regards the the sex-gland albumin as being specific of dementia precox.

#### Kottmann's Reaction

Considerable attention has been directed to the "Kottmann's" reaction" in psychiatric cases, particularly since this reaction has been reported upon recently by Raphael and Smith<sup>11</sup>. The reaction was first described by Kottmann in 1920, who observed that serum from normal individuals rapidly reduces colloidal iodide of silver to metallic silver. He found that the reaction was greatly retarded in hyperthyroidism, which he interpreted as due to the fact that "serum from these patients has an increased power to protect the colloidal iodide of silver against reduction to metallic silver." He found also that the reaction appeared to be hastened in certain cases of hypothyroidism.

Raphael and Smith tested out the reaction in 291 cases of psychosis, of which 87 were schizophrenic cases, and reached the conclusion that, "the reaction seems to be dependent on the emotional state, as they found positive reaction during maniacal and catatonic attacks, whilst the reaction progressed normally in calm periods." Thus offering evidence that there is an increased thyroid function during periods of excitement.

It will be recalled that Kraepelin found the pupils of dementia precox cases dilated during the first stages and during excitement. This observation has been confirmed in a general way by such observers as Schule<sup>12</sup>, Schultz<sup>13</sup> and Weiler<sup>14</sup>.

Almost every observer of dementia precox cases has noted changed conditions of the circulation, pulse, and blood pressure. Thus, Kraepelin found low blood pressure the rule, with varying pulse rates. Meyer<sup>15</sup> also found both bradycardia and tachycardia; while Klipstein<sup>16</sup> and Knapp<sup>17</sup> mention tachycardia as a symptom in the hebephrenic type. On the other hand, although

Goldstein and Reichmann<sup>11</sup> found that bradycardia was very characteristic of catatonia, they found the frequency of the pulse normal in hebephrenia. But here, again, the exact or approximate stage of the disease was not carefully studied.

#### Circulatory Changes

Cyanoses, cold hands and feet and other vasomotor disturbances in dementia precox cases have been observed for a long time and generally attributed to anomalies in the visceral nervous system. And those closely kindred conditions, increased secretion of saliva and perspiration, are also seen frequently—almost characteristically—in certain types. These are referred to by Huffer<sup>12</sup>, Specht<sup>13</sup> and others. While Knapp<sup>14</sup> found increased salivation and hyperidrosis chiefly in hebephrenia, his observation was that these secretions were reduced in catatonia.

Lymphocytosis is found in practically all endocrine disturbances, and hyperleukocytosis is also frequently observed. It is interesting, therefore, that Lundevall<sup>15</sup> found hyperleukocytosis present in most cases of dementia precox, while Kreuger<sup>16</sup> also found it in 70 percent of hebephrenic and in 44 percent of catatonic cases. According to Langfeldt, most observers found lymphocytosis in catatonia.

There seems to be no question that pathologic dermographism is frequently seen in dementia precox, and also low blood pressure. The percentage of cases showing a reduced basal metabolism is also high, especially in the cases of comparatively recent development. But observation on this is still inconclusive, possibly because sufficient attention has not been given to this same time element.

#### Sugar in Blood and Urine

Alimentary glycosuria has been studied by such observers as Trepsat<sup>17</sup> who, in 1905, found alimentary glycosuria after 150 Gm. of glucose an almost invariable symptom in dementia precox; while Schultz<sup>18</sup> and Knauer<sup>19</sup>, a little later, found, in 20 patients, a great number with spontaneous glycosuria, chiefly during catatonic excitement; rarer in hebephrenia.

Langfeldt states that "one of the first to examine the fasting blood-sugar in dementia precox was Heidema", who, in 1919—as a matter of fact in contrast to what most researchers have later come to—found that 10 out of 13 cases had an increased fasting blood-sugar (above 0.11 percent, Bang's method). Most of these cases were characterized by stupor and dis-

couragement. Kooy<sup>20</sup> found (1919), in 10 cases of schizophrenia, values from 0.076 to 0.116 percent; Wuth<sup>21</sup> found (1921), among 40 cases, 15 with increased fasting blood-sugar, the average value in all cases being 0.107 percent. Bowmann, Edison and Bur-lodge found (1922), in 3 out of 10 cases, increased fasting values, whilst Bowmann, in another publication, states that he found normal values (average 0.097 percent), excluding all cases of bodily diseases."

These observations have been confirmed by the experimental work of quite an impressive company of physicians, with evidence that warrants the conclusion that "alimentary glycosuria appears more frequently in this disease than in normal individuals. With regard to the fasting blood-sugar, some authors have found a number of cases where this has been slightly raised, but most cases have shown values within the normal limits, from 0.080 to 0.11 percent. A couple of authors have noted abnormally low values."

#### Sympathetic Involvement

The non-sensitivity of dementia precox cases to subcutaneous injections of adrenalin (epinephrin) has been frequently observed. Such observers as Schmidt<sup>22</sup>, Schultz<sup>23</sup>, Goldstein and Reichmann<sup>24</sup>, and Neuburger<sup>25</sup> seem to regard it as characteristic.

In 1904, Bumke<sup>26</sup> first called attention to the lack of dilatation of the pupil on sensible irritation (the socalled ciliospinal reflex) in a high percentage of dementia precox cases, particularly in catatonia. According to his observations, the pupils failed to dilate in 50 percent, at the climax of psychosis and in all quite demented forms. And since Bumke's initial experiments his observations have been confirmed repeatedly. The weight of evidence shows that it is most frequently observed in catatonia, although Huhner observed it in 75 percent of all cases.

In 1908, Aschner<sup>27</sup> first described a condition of distinct reduction of the pulse frequency by pressing on the eyeball—"Aschner's reflex"—and suggested this as a sign of "a vagotonic disposition." Later such observers as Walter and Krambach<sup>28</sup> found the reaction positive in 6 out of 11 cases of acute catatonia, and in 2 out of 5 chronic cases. Still later, Goldstein and Reichmann<sup>29</sup> found that the reaction was frequently positive in catatonia, although often negative in hebephrenia. And in 1918, Pilz<sup>30</sup> considered a positive Aschner's reaction in catatonic stupor of sufficient importance to be of service in the differential diagnosis of simple depressive stupor.

Another rather significant point was made by Dawson<sup>35</sup> who "found positive Aschner's reactions in all cases that reacted severely to pilocarpin; thus, amongst others, in 7 out of 9 cases of catatonic stupor."

In summarizing the work of Langfeldt, which we have followed extensively in our observations of dementia precox at the Psychoendocrine Clinic, it is apparent that a vast majority of these cases present anomalies, closely, or directly, associated with the endocrine and the sympathetic nervous system.

#### Physical Signs of Dementia Precox

Stated briefly, one may reasonably expect to find, in a majority of cases of catatonic and hebephrenic dementia precox: (1) large pupils, with possibly some light reaction anomaly; (2) low blood pressure; (3) cold, clammy hands and feet, pale or cyanotic; (4) bradycardia or tachycardia; (5) salivation and hyperhydrosis; (6) pathologic dermographism; (7) a negative ciliospinal reflex; (8) a positive Aschner's reflex; (9) a positive Abderhalden (Fauser's) test; (10) probably hyperleukocytosis and almost certainly lymphocytosis; (11) a non-sensitivity to epinephrin; but (12) a hypersensitivity to pilocarpin; and (13) a positive response to the alimentary glycosuria test. In addition, if the patient is twenty or more years of age, a radiograph of the ulna and radius often discloses open epiphyses, indicating gonad involvement. The normal closure time is 18 years.

In short, even if only fifty percent of the above physical abnormalities are found in any given case, we still have a most suggestive group of somatic symptoms that, coupled with the mental symptoms, should be a great aid in diagnosis: Also, in treatment—although that is not so well developed. And last, although by no means least, as Langfeldt points out, "if the somatic symptoms could be proved at such early stages, they could be of importance in forensic psychiatry."

And he concludes, finally: "The constitution that is supposed to lie at the foundation of dementia precox must, of necessity, depend upon a specific inferior endocrine formula. In this essential constitution itself, we have an expression for heredity. The inferiorly constructed endocrine system, besides resulting in the development of the special constitutional type, also results in an inferior development of the brain. When, then, this inferior endocrine system, at puberty or through other accidental causes, is exposed to too great a strain, we get the

acute disturbances which we have seen in the acute phases."

#### References

- 1.—Langfeldt, Gabriel: "The Endocrine Glands and Autonomic Systems in Dementia Praecox." J. W. Eides Boktrykkeri A/S, Bergen, 1926.
- 2.—Kraepelin, E.: "Lehrbuch der Psychiatrie", 8th edition, 1913.
- 3.—Fauser, A.: Pathol. serol. Befunde bei Geisteskranken auf Grund der Abderhaldenschen Anschauungen und Methoden. *Allg. Zeitschr. f. Psych.* 70: 719, 1913.
- 4.—Ewald, G.: Untersuchungen über fermentative Vorgänge im Verlaufe der endogenen Verblödungsprozesse vermittelt des Abderhaldenschen Dialyserverfahrens etc. *Arch. f. Psych. u. Neurol.* 60:248, 1919.
- 5.—Kafka: Ueber den Nachweis von Abwehrfermenten im Blutserum, vornehmlich Geisteskranken, durch das Dialysieverfahren nach Abderhalden. *Zeitschr. f.d.g.N.u.P.* 18:341, 1913.
- 6.—Kottmann, K.: Kolloidchemische Untersuchungen über Schilddrüsenvorprobleme. *Schweiz. Med. Woch.* 1:644, 1920.
- 7.—Raphael, Th., and Smith, G. J.: The Kottmann Reaction as Applied to Psychiatric Cases. *Am. Journ. of Phys.* 4:161, 1924.
- 8.—Schüle: Zur Katatoniefrage. *Allg. Zeitschr. f. Psych.* 54:516, 1898.
- 9.—Schultz: Neue körperliche Symptome bei Dementia praecox. *Münch. med. Woch.* 7:1759, 1914.
- 10.—Weiler, K.: Untersuchung der Pupille und der Irisbewegungen beim Menschen. *Zeitschr. f.d.g. N.u.P.* 18, 1910.
- 11.—Meyer, E.: Körperliche Störungen bei Dementia praecox. *Neurol. Centralbl.* 483, 1912.
- 12.—Klipstein: Ueber die hebephrenischen Formen der Dementia praecox Kraepelins. *Allg. Zeitschr. f. Psych.* 63:512, 1906.
- 13.—Knapp, A.: Körperliche Symptome bei funktionellen Psychosen. *Arch. f. Psych.* 44:709, 1908.
- 14.—Goldstein, K. and Reichmann, F.: Ueber die körperlichen Störungen bei Dementia praecox. *Neurol. Centralbl.* 33:343, 1914.
- 15.—Hüffler: Ueber die kataton. Anfälle. *Jahresvers. d. Deutsch. Vereins*, April 24, 1908; etc. *Allg. Zeitschr. f. Psych. u. Neurol.* 56, 1908; etc. *Neurolog. Centralbl.* 65, 1908.
- 16.—Specht, G. and Müller, L. R.: "Die Lebensnerven", 2nd edition, Berlin, 1924.
- 17.—Op. cit. 13.
- 18.—Lundvall, H.: Blodundersökningar pa sinnessjuka. *Hygios* 69:1142, 1907.
- 19.—Krueger: Ueber die Cytologie des Blutes bei Dementia praecox. *Zeitschr. f.d.g.N.u.P.* 14:101, 1912.
- 20.—Trepasat: Consid. des troubles physiques dans la démentie précoce. Th. de Paris, 1905. Cit. by Reiter, vide 298.
- 21.—Schultz and Knauer: Störungen des Kohlehydratstoffwechsels bei Geisteskranken. *Allg. Zeitschr. f. Psych. u. Neurol.* 66:761, 1909.
- 22.—Op. cit. 21.
- 23.—Heidema, S. T.: Blutzuckerbestimmungen bei psychiatrischen und neurologischen Patienten. *Zeitschr. f.d.g.N.u.P.* 48:111, 1919.
- 24.—Kooy, F. H.: Hypoglykaemia in Mental Disorders. *Brain* 42:214, 1919.
- 25.—Wuth, O.: Der Blutzucker bei Psychosen. *Zeitschr. f.d.g.N.u.P.* 64:83, 1921.
- 26.—Schmidt, V.: Adrenalinunempfindlichkeit der Dementia praecox. *Münch. med. Woch.* 7:367, 1914.
- 27.—Op. cit. 9.
- 28.—Op. cit. 14.
- 29.—Neuburger, K.: Ueber die Wirkung subcutaner Adrenalininjektionen auf den Blutdruck bei Dementia praecox. *Arch. f. Psych. u. Nerv.* 55:521, 1915.
- 30.—Bumke: "Die Pupillenstörung bei Geistes- und Nervenkrankheiten." Jena, 1904. Cit. by Wassermeyer. *Arch. f. Psych. u. Neurol.* 43:124, 1908.
- 31.—Aschner, B.: Ueber die Funktion der Hypophyse. *Pflügers Archiv.* 146:1, 1912.
- 32.—Walter, R. and Krambach, R.: Vegetatives Nervensystem und Schizophrenie. *Zeitschr. f.d.g. N.u.P.* 28:232, 1915.
- 33.—Op. cit. 14.
- 34.—Plez, A.: Ueber ein Bulbusdruckphänomen bei der Dementia praecox. *Psychol. neur. Woch.* 18: 361, 1927; etc. *Zeitschr. f.d.g.N.u.P.* 15:70, 1918.
- 35.—Dawson, W. S.: A Study of the Endocrine-Autonomic Disorders of Dementia Praecox. *Journ. of Ment. Sc.* 60:182, 1923.

# Liver Substance Implantations and Hypertension

By L. L. STANLEY, M.D., F.A.C.S., San Quentin, Calif.

RECENTLY considerable excitement was produced by the statement that a certain fraction of liver would cause a marked drop in blood pressure. Although subsequent studies have tended to dissipate some of this early enthusiasm, it was felt that it would be interesting to see what effect the subcutaneous injections of whole macerated liver substance would have.

Eight prisoners with known high blood pressure were selected. Readings were carefully taken for two to three weeks before the treatment, to obtain their normal pressures. Both systolic and diastolic were taken on these patients by the same observer between twelve and one o'clock each day.

Only five of the patients were given liver substance implantation, one was given an implantation of testicular substance, while two were used as controls.

The liver of a rabbit was removed aseptically immediately after death. This was ground up in a small, sterile meat chopper, to the consistency of tooth paste. With a metal syringe similar to that used for testicular substance implantations, this liver material was injected under the skin of

the abdomen, radially from the point of puncture. About 4 cc. were given on either side.

The graphs show the pressures taken on February 15th, 1927, and also the average for each ten-day period following.

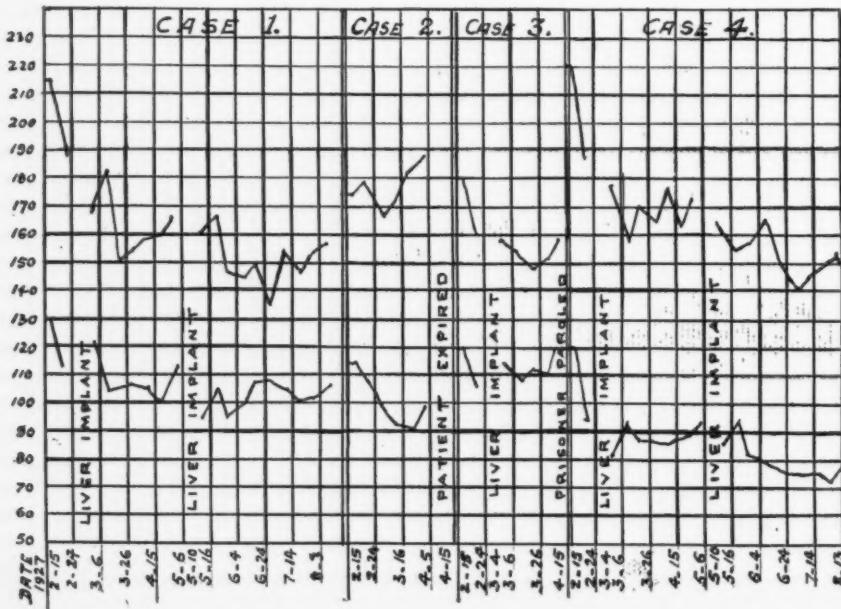
## Case Reports

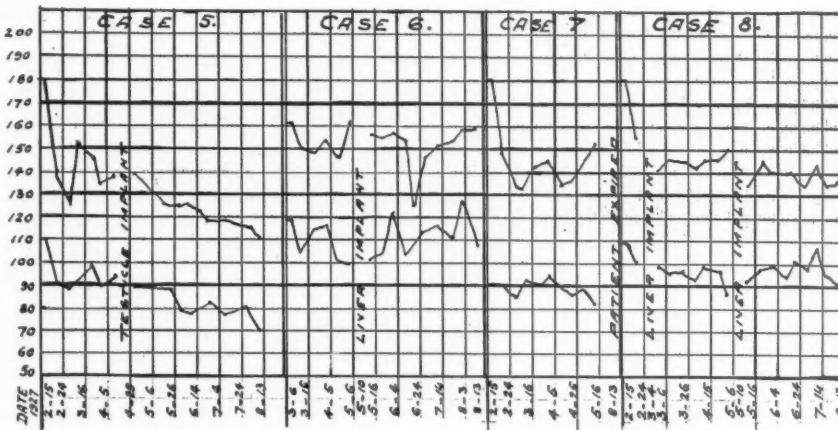
*Case 1.*, was a laborer, age 65. He had never been ill. His complaint on entering prison, in May, 1926, was headache and dribbling of urine. Physical examination showed him to be moderately nourished and developed, weighing 147 pounds. He had dentures. His heart and lungs were normal. The prostate was enlarged and firm. There were marked varicose veins and arteriosclerotic changes, with evidences of senility. The Wassermann test was negative.

On March 4, he received a liver substance implantation. His temperature rose to 100.5° F. and remained so, with remissions, for four days. The site of the implantation became reddened, swollen and painful. Suppuration took place and lasted for 10 days.

On May 10, he was given a second treatment. With this he had fever, with suppuration and discharge of pus.

From the graph it is seen that the pressure was lowered by this agent. The patient gained 18 pounds in weight and said that his headaches had disappeared.





Case 2, was 72 years old and a laborer by occupation. He had never been ill and had been in prison over seven years. On December 4, 1925, he had entered the hospital complaining of pain in the chest, dizziness and dyspnea. His blood pressure on this date was 175/100. Together with a diastolic murmur heard in the aortic area, he had an irregularity of the heart beat. His weight was 205 pounds. Daily blood pressure readings were begun on February 15, 1927. On March 8, paralysis developed on the left side, but he was not rendered unconscious. He gradually developed edema of the extremities and died on April 13.

In this case no liver treatment was given. He served as a control.

Case 3: Aged 32, was an accountant. His father died at age 54 years of "high blood pressure." He weighed 185 pounds and claimed never to have been ill. His blood pressures, taken at various times were:

January 10, 1926.....	210/160
March 23, 1926.....	194/130
June 16, 1926.....	210/150

No cause for his hypertension could be found.

On March 4, 1927, he was given a liver substance implantation. From the graph it is seen that his pressure was lowered 10 mm. after the treatment, but returned to 158 systolic just before he left the prison in April.

Case 4: Farmer, age 64, first sought medical attention in January, 1926, when he was brought to the hospital complaining of shortness of breath and spastic paralysis of left arm and leg. At that time his pressure was only 136/80.

On February 15, 1927, his tension was 220/120, but during the next ten days it averaged 187/93. A liver substance implantation was given on March 4. There was a slight local reaction without fever. A second treatment was given on May 10.

From the graph it is seen that the blood pressure was definitely lowered following the implantation.

Case 5: Farmer, aged 66, had a general arteriosclerosis. In August, 1919, he was in the hospital three days because of dizziness, constipation and precordial pain. His weight then was 128 pounds. In August, 1924, he complained of the same symptoms, as well as of occasional fainting spells. His blood pressure was 170/112. He was confused and disoriented. A diagnosis of senility was made.

On February 15, 1927, his pressure was 180/110, but this varied, so that the average for the next ten days was about 145/90.

On April 7, he was given an implantation of testicular substance. His graph shows that his blood pressure markedly decreased. No liver substance was given him.

Case 6: Electrician, age 30. He had never been ill. On entrance to prison, in 1926, he weighed 220 pounds and his blood pressure was 154/88. The Wassermann test was negative.

In February, 1927, a left, recurrent, inguinal hernia was repaired under spinal anesthesia. His weight had, without known reason reduced, to 147 pounds, stripped. There appeared slight traces of albumin in his urine, and his blood pressure was 172/130. The average from March 6, to May 10, the time of the liver implantation was about 155/105.

It is seen from the graph that the average blood pressure was only slightly decreased following the treatment.

Case 7: Man, 80 years of age, came to prison in 1919. In 1925 he suffered from tachycardia, accompanied by marked weakness and subnormal temperature. This cleared up within a few days.

In May, 1925, he had a similar attack and was assigned to the infirm ward. His arteries were markedly sclerotic and his blood pressure averaged 140/70 at that time.

The graph shows his pressures. No liver implantation was given. In May, 1927, he had a stroke of paralysis and in August he died of pneumonia. This case is cited

merely as a control. The tendency of his pressure was upward. It, in itself, seemed scarcely high enough to cause the paralysis.

*Case 8:* Carpenter, age 57. He had had malaria and rheumatism. He denied venereal diseases and his blood Wassermann test was negative. His cerebrospinal fluid, however, gave a strongly positive reaction.

In March, 1926, he was given neosalvarsan (neoarsphenamine) and fluid removed from the spinal canal. After several such treatments his cerebrospinal fluid became negative.

On March 3, 1927, he was given a liver substance implantation. There was some inflammation but no suppuration.

A second treatment was given on May 10. The patient left the prison in August.

The graph shows a slight lowering in the blood pressure.

#### Summary

Of the five patients given liver substance implantations, all had a slight lowering of blood pressure. Two who were used as controls died following strokes of paralysis, although one had no hypertension.

One control given testicular substance had a more pronounced lowering of blood pressure than did those given the liver.

There was a local reaction at the site of implantation in all.

These experiments are by no means conclusive but are sufficiently productive of results to encourage further investigation.

## Endocrine Gland Surgery

By MAX THOREK, M.D., Chicago

Surgeon-in-Chief, The American Hospital, Chicago.

ALTHOUGH in the past few years there has been no startling development in the surgical technic of endocrine gland transplantation, the end-results of established surgical methods, so far as they have been observed, have been excellent, and prove that, in experienced hands, glandular transplants have a definite place in therapeutics, with constantly increasing indications.

Sex gland transplantation has received the greatest amount of attention from surgeons, and the various technical procedures have been so worked out and perfected that these operations have been reduced to a routine matter. One must, of course, be fully conversant with the technic of the operation one wishes to undertake.

#### Ovarian Implants

The early results of Tuffier in *ovarian transplantation*, showed that good results might be expected, in well-selected cases, from both homeoplastic and autoplastics transplants. He was a pioneer in the practical application of this type of organic transfer, and found that, in women whose ovaries had been removed, periodic menstrual function continued from five to ten years following proper implantations. When this did not occur it was due to the fact that the transplanted ovary was either pathologic, or the donor was of advanced years. Ovarian tissue, removed two to three years after transplantation in the abdomen, showed vascularization and the production of corpora lutea.

Among the more recent work and reports on this subject, only those of Magian and Schultze will be cited, bearing in mind that most of the transplantations carried out by these operators have been in cases where the existing ovaries were functionally deficient but had not been removed.

Magian, before the London Surgical Society, reported that for ten years he had been executing homogeneous ovarian transplantation, and that in all cases there was more or less success, while some women who had been childless before this procedure became pregnant. In other cases, effects were observed which were similar to those that followed the Voronoff testicular transplantations in the senile male. That is to say, there was restoration of physical fitness, female characteristics, attractiveness and vivacity. Magian's results were based on his observations in 100 operations.

Schultze reported permanent success (from two and a half to six years) in 42 percent of a series of thirty-eight cases in which a homeoplastic ovarian transplantation had been done because of ovarian insufficiency. Of these thirty-eight women, nine became pregnant. In young, castrated women the permanent results were not so good, as in many cases the menstruation was irregular and scant, and ceased after about one and a half years. For those who are particularly interested in this work I can heartily recommend the recent book of Vittorio Pettinari on ovarian

transplantation. It is a splendid book, and its originality and comprehensive bibliography make it truly worth while.

As in Tuffier's cases, Schultze found that, in general, the age of the transplanted ovary has much to do with the functional results. The best results were observed when the ovaries were taken from women between the ages of twenty-five and thirty-five years. In no case does the transplanted ovary begin to show results until about six months following the transplantation, after which it passes through the regular monthly congestion and discharge of hormone into the blood, which Schultze believes is the important causative factor in menstruation.

#### Testicular Implants

Now that the undesirable and harmful newspaper publicity in regard to *testicular transplantation* has ceased, the surgical value and importance of this procedure can be calmly evaluated by physicians and surgeons. The main points in the development of this procedure are: (1) That a testicle transplanted in the supraperitoneal space, just beneath the rectus abdominis muscle, will, in many cases, live, become vascularized and function, producing the same constitutional effects as the normal interstitial testicular tissue. The reasons on which this technic is based will be found fully described in my book on "The Human Testis," published in 1924; (2) That heterografts from the higher anthropoids, having a blood affinity, which can be scientifically demonstrated, with the human being can be used and will, in well selected cases, function identically with human homeografts; (3) That, although such grafts do not "rejuvenate" in the commonly accepted sense, they are often capable of restoring, for a comparatively long period, lost physical and mental vigor, and sexual capacity to a greater or lesser degree. One must not expect that senility and organic changes developed on that basis can be restored to a youthful condition. It is for that reason that I have emphatically objected, in my articles on this subject, to the use of the term "rejuvenation".

Retterer recently removed a transplant from a man aged seventy-one, who had been operated upon by Voronoff three and a half years previously. The man was in better physical and intellectual condition at the age of seventy-one than he had been at sixty-seven. Histologic examination of

the transplant showed very slow transformation of its epithelial tissue into connective tissue, and its functional activity in producing hormone was only becoming exhausted at the end of three and a half years. A similar transplantation could again be done.

To cite from the mass of evidence regarding the "taking" and functioning of implants from the higher anthropoids to man would only obscure the point. I will merely say that the value of testicular transplantation in the restoration of lost sexual and physical activity has been recognized by the French government, which has officially sanctioned such procedures in old cattle at the government experimental farms in Algeria and elsewhere.

The physiologic results obtained from testicular transplants are due either to the slow resorption of the graft, which constitutes a kind of autolytic ophotherapy, or to the endocrine role of the intrainterstitial elements which the testicular resorption has created in the tissue of the host.

#### Implants of Other Glands

The use of fragmental *thyroid implants* has been known since 1884, but successful partial transplants of *thyroid and parathyroid tissue* were not reported until 1906 and 1907 by Payr, Biedl and Carrell and Guthrie. Since that time the results from these procedures have varied. Recently Bogoras has reported the transplantation of thyroid tissue from a woman aged twenty-eight, who had exophthalmic goiter, into a cretin. The right half of the thyroid gland was used, and the superior thyroid artery of the transplant was sutured to the common carotid of the recipient. Signs of improvement in the condition of the cretin appeared a few weeks later, and after six months the improvement was quite marked. Physically and psychically there was evidence of a complete change, and apparently the transplanted gland was functioning. There are several similar reports in the literature.

Successful transplantation of the *suprarenal cortex*, in guinea pigs, has been reported by Jaffe. Autoplastic transplants were placed in the abdomen in these cases. Homeoplastic transplants were found to degenerate after a few months. It has been found that small autoplastic suprarenal implants can maintain life in completely suprarenalectomized animals for a considerable period, and large transplants

maintain life and a good condition indefinitely.

Transplantation of *pituitary and pancreatic tissue* has been done, but the conclusions thus far drawn from these efforts are fragmentary and incomplete. Professor Durante, at the request of the well known Italian endocrinologist, Nicola Pende, recently made a pluriglandular transplantation in a woman aged sixty-seven, who had not menstruated for twenty years. Durante implanted under her breast ovarian, parathyroid and hypophyseal tissue, taken from a macacus, and a few months after this operation the patient began cyclic monthly menstruation, which still continues.

I was pleased to note the statement in a recent issue of *Minnesota Medicine* (June, 1928) that there are signs that endocrinology as a science is coming of age.

"The isolation of the parathyroid hormone, the discovery of the estrum-producing effect of the liquor folliculi, and the preparation of a growth-accelerating substance from the anterior lobe of the hypophysis, are especially significant of progress in this field. The recent work of Kamm and his collaborators, who have separated posterior pituitary extracts into oxytocic and pressor fractions, may make possible more exact determinations of the normal functions of the pituitary body.

"Rogoff and Stewart, after years of pa-

tient work on the suprarenal gland, have prepared a substance from the cortical portion of the gland which prolongs the lives of dogs on whom suprarenalectomy has been performed, and which is also giving encouraging results in the treatment of Addison's disease.

"The growing interest of scientists in fundamental endocrinology is attested by the large number of valuable contributions presented at the recent meeting of the Federation of Biological Scientists. Contributions such as these represent the results that can be obtained when exact and accurately controlled methods of experimental medicine are brought to bear on the problems of the internal secretions".

To sum up, it appears that, in the various endocrinopathies, transplantation is ascending to a legitimate place in therapy. If quacks, "rejuvenation experts," and the unscrupulous can be dissociated from this work, and the lay press can be made to cease its misrepresentations regarding this field of endeavor, unbiased, scientific workers will be given a better opportunity to work, unharassed by sensation seekers, and humanity can be better served, while the memory of Brown-Séquard may be sanctified as the first man who fearlessly picked up the torch of truth and threw its rays into the darkness of this unexplored field.

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## Reactivating the Aging Female Organism by Endocrine Support

By HARRY BENJAMIN, M.D., New York.

**I**N a recent publication<sup>1</sup> I have given the following list of methods, used for the purpose of preventing and retarding the process of aging. For the sake of a general survey of the entire problem, I may be allowed to reproduce this list here.

### "Rejuvenation" Methods

(Better named "reactivation", "re-energization" or "restoration").

- A. Indirect preventive (non-specific method, equal to "preservation of youth"). General proper living, with proper health examinations.
- B. Direct, therapeutic, "specific" method (equal to "rejuvenation").
- I. Not utilizing sex glands (gonads).
  - a. Diets
  - b. Sun baths
  - c. Radium emanation
  - d. General diathermy

- e. Blood transfusions and injections
- f. Cosmetic operations and treatments
- g. Special mental and physical exercises, etc.
- II. Utilizing sex glands or gonads (testicles, ovaries).
  - a. Foreign gonad
    1. Transplantation of human gland
    2. Transplantation of monkey gland
    3. Transplantation of animal gland, not related to human species
    4. Injection of fresh testicular substance
    5. Injection of testicular or ovarian extract.

- b. Individual's own gonad
  - 1. Vasoligation (Steinach Operation)
  - 2. Albugineatony (Steinach "Repetition Operation")
  - 3. Chemical elimination of Sympathicus (Doppler Method)
  - 4. X-ray radiation
  - 5. Radium radiation (?)
  - 6. Diathermy
  - 7. Auto-transplantation

man

man  
and  
woman

I am not concerned here with the indirect, preventive, non-specific measures; neither am I concerned with the various operative procedures devised to reactivate the aging male organism. The latter method has received a great deal of attention in recent years, but the problem of combating old age in women has been neglected, to a large extent, in the medical literature. This may be due to the fact that reactivation methods in women are easily confused with cosmetic procedures and beauty-parlor activities, a discussion of which the majority of physicians would consider below their dignity.

On the other hand the problem of reactivation of the female organism is a much more complex one than the corresponding procedure in men. For the latter we have some plain operative procedures, for instance, the vasoligation or so called "Steinach operation". No method that is so universally applicable is available for women, but we have a number of procedures at our disposal, the proper combination of which can accomplish results similar to those of the Steinach operation in men. Occasionally the results are even more dramatic and impressive than those from vasoligation<sup>1</sup>.

While the underlying principle for all reactivation methods in men consists in a general hormone mobilization, by reactivating the gonadal function, the principle for the corresponding method in women, as I have used it during recent years, is slightly different. Activating gonadal function is indeed the most important task to be accomplished, but it is not done only by directly influencing the ovaries through ovarian therapy, but the pituitary is also called upon to act as activator of the gonads and thus influence ovarian function in an indirect way.

We can differentiate four distinct methods devised and used for reactivating the female organism. One is operative, the other three

are non-operative in nature. Of the latter methods, either one can be used singly or in combination with one or both other methods.

#### Ovarian Transplantation

The operative procedure is the transplantation of ovaries\*. The entire ovary or part of one can be transplanted and the material is taken from human beings as well as from various animals.

The ovary taken from an animal not related to the human species, could under no circumstances heal in and become vascularized. A clinical result from such a transplantation is denied by the majority of authors. The transplanted gland is absorbed, unless sloughing or abscess formation should occur. During the time of absorption an hormonal effect may be noticeable and may even persist for a while, by having given a certain impetus to the patient's own glands. A number of authors have reported results with this method, among others, Hunt<sup>12, 13</sup>, with the ovaries of sheep, and Serdjakoff<sup>14</sup>, with goats' ovaries. It is, however, still a question whether these results are specific or are due to the absorption of a foreign protein.

The ape ovary may take a longer time to be absorbed and may therefore exert a somewhat prolonged clinical influence, although Voronoff, who introduced the ape gland transplants, has given up the method with ovaries as unsatisfactory (verbal communication).

There is no doubt that the only operative procedure which offers chances for a definite and lasting result is the grafting of a human ovary, taken from a young woman, complete or in part, and usually transplanted while still warm (homio-transplantation). Auto-transplantations have also been used; i.e., the transplantation of the removed gland to the same patient. Various authors have reported various methods in their technic and have given various indications. The majority recognized as one of the principal indications the climacterium and beginning old age.

Morris<sup>15</sup>, New York, performed the first ovarian transplantation over 20 years ago and many have followed since. In recent years good results were reported by Bumm-Sippel<sup>16</sup> (Berlin), Loeser<sup>17</sup> (Berlin), Natrass<sup>18</sup> (Melbourne), Stocker<sup>19</sup> (Lucerne), Thorek

\*For detailed information regarding the researches on which the transplantation therapy is based, see A. Lipschütz "The Internal Secretion of the Sex Glands", (Williams and Wilkins, Baltimore).

(Chicago) and others. These results consisted in a relief from the complaints of the menopause, artificial or physiologic; in a general improvement of health and increase of vitality; and the occasional return of libido and menstruation (Sippel). "The clock of life can be turned backward for a while", says Loeser<sup>16</sup>.

There is no doubt that the operation is often effective and, aside from the hazards of any operation, is to be considered void of dangers, provided that the donor is selected with the necessary caution. However, the method can never become universally applicable; only in comparatively rare instances will we have a healthy, youthful individual available and willing to part with one or even part of one ovary.

The discussion of the other three non-operative procedures must necessarily be incomplete, just as the discussion of ovarian transplants constitutes only a brief survey. The principal points alone can be given, together with indications as to the practical applications, because too many branches of medicine are concerned: surgery, roentgenology, electrotherapy, organotherapy, gynecology and cosmetics, not to speak of research work which also enters to a large extent and can only briefly be touched upon. For the same reason only those publications have been mentioned in the bibliography which are directly concerned and in which a more interested reader could find the complete literature of the various subjects.

#### Roentgen Radiation

Of the non-operative methods, the first one is concerned with the use of the roentgen rays in small, socalled stimulating doses. Steinach<sup>17</sup> had already suggested x-ray radiation to revivify the function of the aging ovary, in 1920, and had based this suggestion on experiments which he had carried out, together with Holzknecht<sup>18</sup> (Vienna), in which these authors were able to show that infantile female guinea pigs, subjected to mild x-ray radiation of the ovaries, matured quicker than control animals. Furthermore, Holzknecht had made the clinical observation that many women treated by x-rays for the purpose of destroying uterine fibromas, showed such a remarkable improvement in their general health as could not be explained by the cure of their disease alone. An increase of ovarian function, with the concomitant beneficial effect to the endocrine apparatus,

had to be assumed. Furthermore, the emmenagogue effect of x-ray radiation in young amenorrheic women is well known (Thaler<sup>19</sup>, Borak<sup>20</sup>). Whether these mild radiations of the ovaries act as directly stimulating to their secretory function, as M. Fränkel<sup>21</sup> and others assume, or whether this stimulation is due to the destruction of inhibiting factors (Holzknecht's school), or whether the stimulation is only a foreign protein sensitization, due to the absorption of destroyed tissue, as Robinson<sup>22</sup> believes, shall not be discussed here, inasmuch as a conclusive answer cannot be given.

Wetterer, in the latest edition of his German text-book on "Roentgen and Radium Therapy", refers to the above experiments of Steinach and Holzknecht and says: "Transferring these experiments to human beings, it was shown that after such mild radiations, the internal secretion of the hypertrophied interstitial ovarian gland (Steinach's puberty gland) increased very greatly; the clinical result is shown in the well known 'Steinach effect' in the form of revivification and rejuvenation of the entire organism." Manfred Fränkel<sup>23</sup> has observed this regenerating effect in hundreds of cases; and "good results throughout" were reported by Groedel<sup>24</sup>, in climacteric cases.

The x-ray dose that I usually employ to the aging ovary is about 25 to 33 percent of an erythema dose, which naturally, is only a fraction of the dose administered to the skin. I usually give this dose in 5 or 6 sittings, alternatingly exposing an area of about 20 sq. cm. above the symphysis and above the sacrum. The skin dose will greatly depend upon the distance between skin and ovary and will have to be determined in each individual case. In patients of average size, 90 to 100 percent of an erythema dose has to be divided between the anterior and posterior fields in order to have about 30 percent reach the ovary.

In addition to the roentgen treatment of the ovaries, I have frequently applied the x-ray to the pituitary, especially in those cases where the vasomotor disturbances of the menopause had persisted very long and had not responded to other treatments. As we shall see later on, the pituitary is to be considered the activator or "starter" of the gonads, and a stimulating dose to the pituitary could therefore well explain the fact that the combination treatment is more

effective than the treatment of the ovaries alone.

The pituitary gland is well suited for x-ray radiation, being a glandular organ sensitive to x-rays, situated between nerve tissues which are not easily affected by these rays. The dose that I usually employ in the pituitary treatment is 25 percent of an erythema dose to the skin, 2 or 4 times to each temple, of which about 1/5 would reach the gland (field 4 sq. cm.). Good results have been described by various

later on, diathermy treatment to the pituitary was added, following the same theoretical considerations, and with the same practical experiences as were discussed for the x-ray treatments of the pituitary. I have suggested a special electrode for the pituitary treatments which I have found more useful than all other methods. The accompanying picture (Fig. 1) shows this electrode. The two contact plates are of the same size, therefore both active. Through a slit in the connecting head-piece (which holds the contacts tightly in place by its spring-effect), they are adjustable in all directions.

In other cases I have, simultaneously with the ovarian treatment, applied diathermy to the thyroid, to the adrenals or to the whole face; the latter only where, in addition to the biologic effect, a cosmetic effect was much desired.

Fig. 2 shows an adrenal electrode, the construction of which I had suggested and which has proved useful. The two sides are movable and the entire device acts as the one active electrode. It is placed above the adrenal glands, which can be located by the fact that the center of the kidney is situated approximately behind the twelfth rib. The indifferent electrode should be about 3 to 4 times larger and is placed directly opposite, over the stomach. There may thus be an incidental effect on the pancreas.

In another group of cases, especially those that showed any thyroid deficiency, as determined by basal metabolism read-

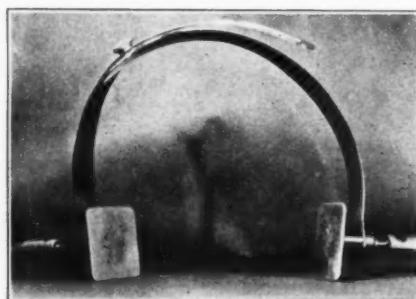


Fig. 1.—Pituitary electrode. The headpiece is insulated from the contacts.

authors, especially by Borak<sup>6</sup>, Werner<sup>21</sup> and Sahler<sup>22</sup> in Vienna.

#### Diathermy

In spite of some very distinct benefits accomplished by x-ray radiation, good results too often alternate with absolute failures and the correct dose is often difficult to determine. It was, therefore, a distinct progress in the reactivation treatment of women when Steinach suggested the production of an artificial hyperemia in and around the ovaries by using the diathermy\* current.

The technic employed in my cases was usually the one advised by Kowarschik<sup>14</sup> (Vienna), in which a belt of tin foil is placed around the abdomen as the indifferent electrode, while the active one is formed by an all-metal vaginal electrode. The dose used was 25 to 30 minutes of a current ranging around 1.5 amperes, daily for about a month. A total of 500 minutes was the minimum applied. It is logical to assume that the hyperemia caused by the diathermy current will increase the function of the ovaries, and the clinical effects have borne out this contention.

In certain cases, which will be indicated

\*Principles and application of Diathermy can be found in G. Bucky's "Diathermy" (McMillan Co., New York).

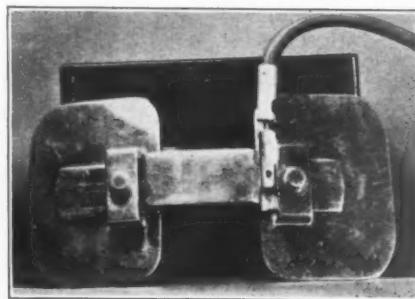


Fig. 2.—Adrenal electrode, nickel plated.

ings, I employed thyroid diathermy. Since it is rather difficult to fit an electrode smoothly over the thyroid region, I usually advise the construction of an individual electrode, after a mould with clay or plaster has been taken. This mould is converted



Fig. 3.—Individual thyroid electrode made after a plaster of paris mould. The connection for the cable is shown on the left. (Silver.)

into a metal electrode and naturally fits absolutely perfectly (Fig. 3). The indifferent electrode is of larger size and is placed between the shoulder blades.

The number of applications and time of each treatment applied to the pituitary, adrenal or thyroid glands depends entirely upon the individual need and must largely be determined by its clinical effects.

It is quite natural that a number of patients undergoing a reactivation treatment are interested in its possible cosmetic effects. A healthier and more youthful appearance has often been observed within a few months following a course of treatment, but in many instances the effect on the facial structures did not fully satisfy the patient. When, in such a case, the repetition of a course of treatment became necessary, after one or several years, or when the appearance of the patient was of paramount importance (for instance, in actresses), a special facial treatment was applied, in

combination with any one of the other methods, including the injection of effective ovarian extract (to be discussed later on).

In order to send a diathermy current equally through all parts of the face, and thus produce a deep hyperemia, an individual facial electrode will have to be constructed. The original one, devised in Vienna, was made somewhat flexible by the use of plaster of Paris bandages (Figs. 4 and 5). The inside of a mask, having openings for eyes and mouth, was laid out with pieces of tin foil. This method proved to be only partially successful. It was unsatisfactory in many instances, because the mask changed its shape too easily and the least defect in the proper contact of metal and skin will cause unpleasant prickling



Fig. 5.—Inner view of mask shown in Fig. 4. The inner surface is more or less wrinkled due to the fact that even thin tin-foil will not smoothly adhere to the curvatures of the mask.

sensations, so that the current can not be applied in sufficient strength.

A later device is an absolutely rigid mask, made after a mould in a similar way as the thyroid electrode (Fig. 6 and 7). With the help of this mask, which insures a perfect contact everywhere, including the mouth and eyes, currents up to 1800 milliamperes could safely be sent through the deep structures of the face without any other sensation to the patient than heat. As indifferent electrode, a large piece of tin foil, is placed under the patient's back.

After 12 to 15 treatments of 20 to 30 minutes each, the first beneficial results are seen in the face, in the form of a clearing of the complexion and smoothing out of the wrinkles. The elasticity, as dependent, in the first place, upon the connective tissue,



Fig. 4.—First type of flexible mask electrode. Outer view.



Fig. 6.—New rigid mask electrode. (Brass, silver or gold.) Outer view.

and then upon the elastic fibers, is definitely increased. This increase can be demonstrated by an instrument (devised by Dr. R. W. Schulte), which measures the skin tension.

This cosmetic discourse was necessary to give a complete picture of reactivation treatments in women, where the cosmetic effects often play such an important part and must be taken into consideration. This local treatment to the face does not seem to constitute an actual endocrine support\*; however, a slight influence is exerted on the thyroid, which is traversed by a part of the current, as it passes from one to the other electrode. I would therefore consider a distinctly overfunctioning thyroid a contraindication for the "mask treatment"; otherwise, if properly employed by a trained person, it is a definitely harmless procedure.

#### Ovarian Hormones

The third, and probably most important, nonoperative procedure for reactivating the feminine organism is the administration of a biologically tested, effective ovarian hormone.

The endocrine function of the ovary is still rather mysterious and very few definite facts are known. It seems well established that the ovary produces more than one hormone — possibly more than two. The principal hormone with which the estrus can be produced in castrated animals (Allen and Doisy test), is the follicular hormone.

\*The psychic effect upon the patient should not be disregarded, as it may have a decided, indirect effect upon the functioning of the endocrine organs.—ED.

It is found, more or less concentrated, in the follicular fluid, in the placenta, in the blood and urine of women after the twelfth week of gestation, in the menstrual blood, etc., and has also been found in small quantities in many other places, even in the testicles and the urine of men, as well as in various plants.

The other hormone produced by the ovary is contained in the corpus luteum and has certain antagonistic functions to the follicular hormone, which can be designated as the ovarian hormone proper. Whether other structures of the ovary, for instance the interstitial cells, have any endocrine function is not definitely known, but probable.

The hormone that alone is able to produce a reactivating effect on the ovary itself and on the rest of the endocrine apparatus is the follicular hormone. Various investigators have succeeded in isolating this active principle. Among the first ones were Allen and Doisy<sup>1</sup>, Frank<sup>2</sup>, Herrmann; somewhat later, Zondek<sup>3</sup>, Lacqueur<sup>4</sup> and Aschheim<sup>5</sup>, in Berlin, and Steinach, Heinlein and Wiesner<sup>6</sup>, in Vienna. For over a year I have been using the socalled Folliculin (Menformon), prepared according to Zondek and Laqueur<sup>7</sup>, which contains 40 mouse units in 1 cc. A higher concentration is used by other authors, for instance by Steinach<sup>8</sup> <sup>9</sup> <sup>10</sup>, but it is denied in some



Fig. 7.—Inner view of mask shown in Fig. 6. The inner surface is smooth except for the reproduction of the skin creases, which can be smoothed out entirely.

quarters that greater concentrations offer greater advantages.

I have employed this water-soluble hormone, the injection of which is absolutely

painless, in about 50 cases, but only in a very few cases alone, without any physical therapy in addition. Those few cases, however, have convinced me that it is of much greater effectiveness and reliability than any other ovarian extract heretofore on the market. I have formerly employed various makes of ovarian extract, in combination with my physical therapeutic procedures, but since I have used the German product, I feel satisfied that the total clinical results are decidedly better. I have usually employed 30 injections, one every day, for one course of treatment, after which a definite clinical effect was accomplished, in the majority of cases.

The future will probably see the employment of an effective extract from the anterior pituitary lobe, to be used in combination with ovarian hormone, but at the present time no such extract is on the market. The recent researches of Ph. E. Smith<sup>11</sup>, in this country, of Zondek and Aschheim, in Germany, and of Steinach and Kun<sup>12</sup>, in Austria, have conclusively shown that the anterior pituitary lobe is the activator or "motor" of gonadal function. It not only produces precocity in infantile animals, but it can also cure eunuchoidism and counteract senility. It has, however, no effect on castrates. The good clinical results in hypogonadal, amenorrheic girls, obtained by x-ray radiation to the pituitary, and the undoubted beneficial effects in relieving symptoms of old age (even if in combination with ovarian therapy), accomplished by x-ray and diathermy to the pituitary, are distinctly significant, in view of the above-cited animal experiments.

#### Classification of Patients

My total experiences with any one or any one combination of the non-operative methods are based on about 250 cases. In determining the method to be used in the individual case, the following points must be taken into consideration: (1) the actual age of the patient; (2) her heredity; (3) her constitutional endocrine make-up; (4) her past history; (5) her present subjective and objective symptoms; and (6) her menstrual situation. The latter is a significant expression of ovarian function and, according to this menstrual situation, I have divided my patients into three classes:

*Class 1.*—Those women who are complaining of a decline in their general vitality, who show signs of premature old age, but who are still menstruating regularly and

present no symptoms of the menopause. If, in these patients, the physical examination reveals no organic defect and, if a diagnosis of an *endocrinasthenia* (often called neurasthenia), especially with hypogonadism, can be made, a reactivation treatment is justified.

If a hypogonadal situation can be assumed, I treat these patients with a series of about 20 injections of ovarian hormone, one every day. The same number of diathermy treatments to the ovaries are given and, in addition, the pituitary or thyroid or adrenals are treated, according to the deficiency any one of these glands may show. If no hypogonadism exists, I dispense with the injections of ovarian hormone, but use diathermy treatments to the ovaries, in addition to the treatment of those glands that show any signs of hypo-function.

Occasionally these latter patients have been simultaneously treated with injections of a polyglandular solution, which I have frequently found to act as a good tonic. Naturally advice is always given as to diet, exercise, etc. No roentgen radiation is used, because the menopause may not be far off and the ovaries at that time are very sensitive to x-rays. Even mild doses may precipitate the onset of the climacterium.

In the following I wish briefly to describe a case, typical for this class of patients:

*Case 1.*—Professional woman, 40 years old, married, no children. First consultation May, 1927. Principal complaint was great physical fatigue, which proved a serious handicap in her work. Sleep very poor, unable to relax. At times backaches, especially severe when fatigue was more pronounced, for instance, during the week following menstruation.

*Past history* negative, except for several attacks of gripe, with following prostration. One brother and one sister have similar attacks of fatigue. Began to menstruate at 13, somewhat irregularly, but never painful. Flow scanty, lasting three days.

*Physical examination:* Fairly well nourished, weight 131, hair prematurely gray. Pulse normal. Blood pressure 115/85. Skin reaction, very faintly red. Basal metabolism test, minus 2. Heart, lungs, etc., negative.

*Diagnosis:* Hypogonadism, endocrinasthenia, premature decline.

*Treatment:* Twenty diathermy treatments to ovaries, ten to pituitary, ten to adrenals, and twenty folliculin injections.

Last re-examination, December, 1927: Feels generally much better. Has "more back of her". Had been working very hard,

but recovered unusually fast from a normal fatigue. Sleep very good, deeper and longer. Hair has become more glossy and she believes that the new hair that has grown is less gray. Menstruation has become regular. No more backache. Weight 132 $\frac{3}{4}$ , blood pressure 120/80. Skin reaction red. Otherwise no change.

An improvement of the ovarian hypo-function has apparently reactivated the endocrine system, especially the adrenal function, increasing the vitality of the organism. Her physician pronounced the result, "very satisfactory".

*Class 2.*—Those who are in the menopause and complain of the various symptoms of this period: hot flushes, sudden perspiration, general nervousness, insomnia, headaches, etc. Menstruation is irregular or has just ceased. Here the reactivation treatment practically corresponds to the treatment of the menopause. The psychic element in these women must not be overlooked, but an organic endocrine basis cannot be denied. In all these cases, daily diathermy treatments to the ovaries and daily injections of ovarian hormone are given. If the symptoms promptly respond to this treatment, no other methods are used. In obstinate cases, however, diathermy and even x-ray to the pituitary are added. The ovaries are usually not subjected to any roentgen treatment unless menorrhagia or some other reason (for instance, a fibroma uteri) should exist to necessitate definite suppression of menstruation by larger doses. In the latter cases, more intense treatment with the ovarian hormone and of the pituitary is usually required.

A brief description of the following case will show the therapeutic value of the ovarian hormone, as compared to other methods:

*Case 2.*—Professional woman, age 50, unmarried, seen first in October, 1927; complained of great nervousness, irritability, frequent depression, failing endurance and many hot flushes with outbreaks of perspiration, even at night, disturbing her sleep.

*Past history* negative. Father died of apoplexy, mother living and well. A maternal relative imbecile; an aunt developed insanity during the menopause. Menses began at 10, regular, moderate flow. First irregularity of menstruation November, 1926. Last menstruation September, 1927.

*Physical examination:* Heart, lungs, abdomen, negative. Pulse 104. Blood pressure 180/115. Basal metabolism +17. Gynecologic examination, negative. Urine, negative. Weight 138 pounds.

*Diagnosis:* Climacterium, hyperthyroidism, essential hypertension.

After having received over twenty diathermy treatments to ovaries and pituitary,

and as many injections of an ovarian extract\*, no improvement was noticed and in December, 1927, the patient still had about twenty hot flushes daily and twelve at night. Was rather depressed and irritable. Pulse 106, blood pressure 170/110.

The patient then received daily injections of Folliculin (40 mouse units) and also Folliculin by mouth. After one month, decided improvement; felt like a "different person"; slept much better, since no hot flushes or perspiration occurred at night and only a few during the day time. Depression has disappeared. Pulse 86; blood pressure 155/110. During the middle of January a short menstruation appeared, scantier than usual.

The patient was last seen at the beginning of May, 1928. Has had normal menstruation in February and in March, but none in April. Felt extremely well and efficient. Occasional slight relapses, with return of some flushes, following nervous excitements; did not disturb her. Was entirely free for two months. Pulse 92; blood pressure 155/95.

The ovarian hormone has doubtless counteracted her climacteric hyperthyroidism, without any other treatment. Her vasomotor instability is not purely psychic, but mainly endocrine. Further courses of injections may occasionally become necessary again. Another logical treatment, in addition, would be roentgen radiation to the thyroid.

*Class 3.*—Consists of the post-climacteric cases, where menstruation has entirely ceased, perhaps for years, and where symptoms of the menopause may or may not persist. These women are usually above 50 or even above 60 years and show signs of a somewhat premature or physiologic senility. If organically well and with no local contraindication, I have always found x-ray and diathermy treatment to the ovaries advisable, but to the largest extent I have relied upon at least 30 injections of ovarian hormone. If necessary, diathermy to individual glands was added, according to constitution and symptoms. Sometimes general diathermy has been found very useful in these cases, especially where the circulation seemed to be impeded. A number of these elderly women, having felt the great invigorating effect from a course of treatment, insist upon repeating such a course of treatment every year or every two years, and there is no doubt in my mind that it keeps them in excellent health and in a condition corresponding to an age of 5 or even 10 years younger.

A typical case is the following:

*Case 3.*—Lady of 62, married, 2 children; has always been tired physically, but during

\*A well known American make was used, since Folliculin was not available at that time.

the last few years excessively and increasingly so. Has not taken the same interest in life as she used to. Outside of occasional frequent urination, no other complaint.

Both confinements with instruments, last one followed by sepsis. Both parents died very old. Otherwise past and family history negative.

Began to menstruate at 16, regularly. Menopause at 39 without any disturbances.

*Physical examination:* October, 1924: Heart, systolic murmur over mitral, no symptoms of decompensation; lungs and abdomen negative; urine negative; pulse normal; blood pressure 175/105; skin reaction, absent; hemoglobin 70%; weight 125 pounds.

*Diagnosis:* Senility; constitutionally, hypothyroid and hypogonadal.

*Treatment:* From October, 1924 to January, 1925, 6 x-ray treatments to ovaries, in all about 30 percent of an erythema dose to the glands. Simultaneously, each time, a mild stimulating treatment to the thyroid (3 to 10 percent to skin). During January, 1925, twenty diathermy treatments to ovaries; no injections of gland extracts. (Ovarian transplantation was refused).

Re-examination, May, 1925 (4 months after finishing treatment). Patient looked and felt much better. Has been able to play strenuous games of golf without undue fatigue. Believes she "never felt so well in all her life." Blood pressure 140/90; hemoglobin 75%, weight 132 $\frac{1}{4}$ .

Examination in June, 1926, showed no marked difference, except a slight gain in weight (136 $\frac{1}{2}$ ) and in hemoglobin (80%).

Exactly a year later the patient was seen again. Had kept most of her gains, but some feelings of tiredness had returned. She requested another course of treatments. Physical examination showed no marked changes, but her systolic blood pressure had increased again to 160. Weight 135. Skin reaction faintly red.

During June and July, 1927, second course of treatment: 3 x-ray radiations of the ovaries—a total of 21 percent of an erythema dose reaching the gland. Twenty injections of Folliculin (40 m. u.) and alternating general and thyroid diathermy.

Responded very favorably, felt exceedingly well all summer.

Last seen in May, 1928. Patient is now 66 years old. Claims to have decidedly more endurance and to be enjoying life more than in many years. Looked unusually well. Blood pressure 135/85. Skin reaction, faintly red.

Off and on during all these years, patient had taken small doses of thyroid and polyglandular extracts by mouth, but they have been unable to check the signs of decline that had appeared in 1924 and again in the spring of 1927. (Her husband underwent the Steinach operation after having seen the favorable result in his wife).

#### Summary

Reviewing all my cases, I must say that there have been very few where the treat-

ment had no beneficial effect whatsoever. Absolute failures, for whatever reason, were not observed in more than 10 percent. The character of the treatments makes it very apparent that they cannot possibly do any harm. The definite successes are about 80 percent; that means that, in 80 percent of the cases, not only subjective, but objective signs of reactivation could be demonstrated.

The subjective symptoms of aging patients are too well known to require a detailed discussion. Complaints as to frequent and easy exhaustion, insomnia, inability to concentrate, general irritability, lack of appetite, etc., are in the foreground.

Among the objective symptoms, the essential hypertension has responded most favorably. Even hypertension with chronic interstitial nephritis has occasionally been considerably reduced.

Statements as to the improved growth of hair have been no rarity. A dry skin has often changed considerably for the better and the skin reaction frequently indicated an improved thyroid function.

In several cases I have distinctly observed an improvement in eyesight and hearing.

The weight has been decidedly influenced. Some patients who had grown stout when approaching the menopause, lost weight automatically without any specific obesity treatment. Here the obesity was of endocrine origin, which is by no means so in all cases. Some other patients who had been underweight for many years or who were losing weight, had little difficulty in gaining. The change in appearance and general health was sometimes so marked that the patient's physician wrote or came to me to inquire about the treatment that had produced these changes, or that the patient's husband came to undergo the Steinach operation.

From an experience of nearly 7 years and from about 250 patients treated here and abroad, I have been forced to the definite conviction that, with the proper combination of the methods described, a marked improvement can be brought about in the physical and mental condition of aging patients, which should not be called "rejuvenation," but which amounts to a reactivation and restoration of vital functions, resulting in a greater comfort and efficiency, and in a definitely better enjoyment of this period of life.

## References

- 1.—Benjamin, Harry: The Steinach Method as Applied to Women. *M. J. and Record*, Dec. 19, 1923.
- 2.—Benjamin, Harry: The Control of Old Age. *Am. Med.*, June, 1927.
- 3.—Benjamin, Harry: Influence of Roentgen Rays on the Endocrine Glands. *M. J. and Record*, Dec. 17, 1924.
- 4.—Benjamin, Harry: "Altersbekämpfung durch Keimdrusentherapie." Verh. d. I. Intern. Congr. f. Sexualforsch., Bd. 2. Marcus and Weber Verl., Berlin, 1926.
- 5.—Borak, J.: Roentgentherapie und Organotherapie bei innersekret. Erkrankungen. *Strahlentherapie*, Bd. 20, 1925, p. 31.
- 6.—Borak, J.: Therapeutische Erfolge durch Roentgenbestrahlung der Hypophyse. *Jahresk. f. aerztl. Forth.*, August, 1924.
- 7.—Dolby, Ralls, Allen and Johnston: The Extraction and Some Properties of an Ovarian Hormone. *Jour. Biol. Chem.*, Oct., 1924.
- 8.—Frank, Robert T.: Function of the ovary. *Am. J. Obst. and Gynec.*, Vol. 8, No. 5, Nov., 1924.
- 9.—Groedel, Franz: Die Roentgenbehandlung klimakterischer Erscheinungen. *Muench. Med. Woch.*, No. 12, March 24, 1922.
- 10.—Fraenkel, Manfred: Die Bedeutung der Roentgen-Strahlen in der Medizin mit besonderer Einwirkung auf das endocrine System. *Strahlentherapie*, Bd. 12, 1921.
- 11.—Fraenkel, Manfred: "Die Verjüngung der Frau." Ernst Bircher, Bern, 1924.
- 12.—Hunt, H. L.: Experiences in Gland Transplantation. *CLIN. MED.*, December, 1923.
- 13.—Hunt, H. L.: The Climacterium in Women. *Med. Times*, June, 1927.
- 14.—Kovarschick, J.: "Die Diathermie". J. Springer, Berlin.
- 15.—Laqueur, Ernst: Ueber weibliches Sexualhormon im bez. des Menstruon. *Klin. Woch.*, No. 9, Feb. 26, 1927.
- 16.—Loeser, Alfred: "Die Wirkung der Eierstocküberpflanzung auf die infantile, innersekretorisch kranke und alte Frau." Verh. des I. Internat. Congr. f. Sex. Forch., Bd. II, 1926.
- 17.—Morris, R. T.: A Case of Heteroplastic Ovarian Grafting. *Med. Rec.*, N. Y., Vol. 69, 1906.
- 18.—Nattrass: Autoplastic Ovarian Transplantation. *Brit. M. J.*, June 23, 1923.
- 19.—Robinson, M. R.: Effect of a Castration Dose of Roentgen Rays upon the Rabbit Ovary. *Am. J. Roent. and Rad. Therap.*, July, 1927.
- 20.—Sahler: *Wiener Klin. Wochenschr.*, No. 15, April 17, 1924.
- 21.—Serdjakoff, M. G.: Heterotransplantations de l'ovaire dans divers endocrinopathies. *Rev. Franc. d'Endocr.*, Oct., 1926, No. 4.
- 22.—Slopel, Paul: Die Ovarientransplantation bei herabgesetzter und fehlender Genitalfunktion. *Arch. f. Gyn.*, Bd. 118 H. 3.
- 23.—Smith, Ph. E.: The Disabilities Caused by Hypophysectomy and Their Repair. *J.A.M.A.*, Vol. 88, January 15, 1927.
- 24.—Steinach, Eugen: "Verjüngung". Julius Springer, Berlin, 1920.
- 25.—Steinach and Holzknecht: Erhöhte Wirkungen der inneren Secretion bei Hypertrophie der Pubertätsdrüsen. *Arch. f. Entw.-Mech.*, Bd. 42, 1916.
- 26.—Steinach, Eugen: Biological Methods Against the Process of Old Age. *M. J. and Record*, Jan. 19 and Feb. 2, 1927.
- 27.—Steinach, Heinlein and Wiesner: Auslösung des Sexualzyklus, Entwicklung der Geschlechtsmerkmale, reaktivierende Wirkung auf den senilen weiblichen Organismus durch Ovar und Placenta extrakt. *Pflueg. Arch.*, Bd. 210, No. 4-5, 1925.
- 28.—Steinach, Kun and Hohlweg: Reactivierung des senilen Ovars und des weiblichen Gesamtorganismus auf hormonalem Wege. *Pfluegers Arch.*, Bd. 219 H. 2, 1928.
- 29.—Steinach, Dohrn, Schoeller, Hohlweg and Faure: Ueber die biolog. Wirkungen des weiblichen Sexualhormons. *Pfluegers Arch.*, Bd. 219 H. 2, 1928.
- 30.—Steinach, E. and Kun, H.: Die entwicklungsmechanische Bedeutung der Hypophysis als Aktivator der Keimdrusenreincretion. *Med. Klinik*, No. 14, 1928.
- 31.—Stocker, S.: "Erfahrungen mit der Keimdrusenüberpflanzung bei Menschen." Verh. d. I. Intern. Sexologen Congresses, Bd. 2. Marcus, Weber Verlag, Berlin, 1928.
- 32.—Thaler, Hans: Ueber Roentgenbehandlung der Amenorrhoe. *Zentralbl. f. Gynaek.*, Nr. 51, June 24, 1922.
- 33.—Werner: *Zentralbl. f. Gynaek.*, No. 31, Aug. 4, 1923.—*Wien. Klin. Wochschr.*, No. 13, Mar. 27, 1924.
- 34.—Zondek, Bernhard: Das Ovarialhormon und seine klinische Anwendung. *Klin. Woch.*, No. 27 und 33, July 2 and Aug. 13, 1926.
- 35.—Zondek, B. and Aschheim, S.: *Klin. Woch.*, No. 6, Nov. 19, 1927.

## How to Kill a Medical Society

*Don't come to the meetings. If you do come, come late. If the weather doesn't suit you, don't think of coming. If you do attend a meeting, find fault with the work of the officers and other members. Never accept office, as it is easier to criticize than to do things. Nevertheless, get sore if you are not appointed to a committee; but if you are, do not attend the committee meetings.*

*If asked by the chairman to give your opinion regarding some important matter, tell him you have nothing to say. After the meeting, tell everyone how things ought to be done. Do nothing more than is absolutely necessary, but when other members roll up their sleeves and willingly and unselfishly use their ability to help matters along, howl that the organization is being run by a clique. Hold back your dues as long as possible, or don't pay them at all. Don't bother about getting new members.*

—The Aesculapian.

# The Seminar

[NOTE: Our readers are cordially invited to submit fully worked up problems to the *Seminar* and to take part in the discussion of any or all problems submitted.

Discussions should reach this office *not later* than the 1st of the month following the appearance of the problem.

Address all communications intended for this department to *The Seminar*, care CLINICAL MEDICINE AND SURGERY, North Chicago, Ill.]

## Problem No. 6

Presented by Dr. Max Thorek, Chicago  
(See CLIN. MED. AND SURG., May, 1928,  
p. 342)

**Recapitulation:** A young physician, engaged to be married, was struck by a shell fragment, in France, and completely castrated.

When seen, he had lost his sex potency and desire and was rapidly losing his male secondary sex characters. Aside from these changes and the fact that he was introspective and depressed, and much disturbed over his marriage contract, he seemed to be entirely normal, mentally and physically.

**Requirement:** What would you recommend and do for a patient in this condition?

Discussion by Dr. E. I. Raymond,  
Wellington, Colo.

I would feed this man some reliable preparation of Leydig cells for the rest of his life. My experience with Leydig cell therapy has been confined to the loss of function in diabetes and in senility.

The Leydig cell therapy does not restore function to any great extent, but it does restore the mental balance so evidently impaired in these conditions. If it will do that in this case it will do all that this man needs.

Discussion by Dr. Chas. E. B. Flagg,  
San Antonio, Texas

Sublimation of his lost sex desire should be encouraged, and some method for the accomplishment of this purpose devised. If he is of the Roman Catholic faith he could enter the priesthood.

His marriage contract with a normally sexed woman would be legally voidable, and if entered into would not conduce to the lasting happiness or contentment of either party.

The transplanting of two testicles, preferably from two healthy, living subjects, into the scrotal stump, should give him relief, at least temporarily, and in the meantime, the administration of testicular extract, hypodermically as well as by mouth, would be in order.

Discussion by Dr. J. F. Roemer,  
Waukegan, Ill.

The first line of attack in this case should be by psychotherapy, rather than ophotherapy. The patient must be brought to see that sexual intercourse is not all there is to love and the married state.

The viewpoint of the lady in the case should be ascertained and her feelings and wishes consulted. If she loved him before he went to war, she probably loves him still and always will do so. To her, he is just as he always was.

The patient must be convinced that while, as a *male*, he is now a nondescript; as a *human being* he is just as much a man as he ever was, and should hold up his head as he always did, look the world in the face and say, "I am a man."

When this readjustment of his psychic outlook has been accomplished, and not before, he is ready for the administration of any of the hormones, separately or combined, that may seem to be indicated.

His treatment should be directed by a physician who is also a *trusted friend*, and should be worked out with intelligence and discrimination; not administered blindly and haphazard.

Solution by Dr. Geo. B. Lake, Chicago

This problem presents two important aspects: one for the endocrinologist and the other for the psychopathologist. The former has been considered by two of the discussants and will be dealt with in detail by Dr. Thorek; the latter has been stressed by Dr. Roemer and alluded to by Dr. Flagg. It is the psychic aspects of this problem which interest me particularly—but, of course, the psyche is intimately connected with the autonomic nervous system and the glands of internal secretion.

The "sublimation of sex desire" is a phrase which is used more and more frequently, and but little understood. The sex urge is the urge to *creative* activity,

not merely to *any* kind of activity; and, while heavy, exhausting physical labor may abolish sex desire, temporarily, by causing somatic fatigue, the only way to sublimate or substitute the natural satisfaction of that natural appetite, is by engaging in some form of work which is distinctly creative—the man must *build something*, with his hands or his brain or both, in order to gain vicarious release from his cosmic cravings.

In this case, however, such a situation does not arise, for the patient's sex desire is lost. He is struggling, not with a primal appetite, which would be equally strong if he were alone on a desert island, but with his chagrin at the loss of his "manhood." His problem is sociologic as well as psychic for, on the hypothetical island, his condition would cause him little or no concern.

With regard to the lady who is involved in the discussion, Dr. Roemer's position might be sound, in certain cases, but, I believe, in very few. It is true that many women who have never been sexually aroused would be able to live comfortably and fairly happily with an eunuch who was intelligent, considerate and kindly—provided they did not, later, meet a man who would awaken them in this particular. Such a possibility would always be in the background.

But here, again, the sociologic factor enters. The girl might be able to live a reasonably satisfactory life with this mutilated man, *on a desert island*; but how would she behave and feel under the sly winks and meaning smiles of her friends when she presents her husband, who is, obviously, not all a man (in the usual meaning of the word), having lost his masculine secondary sex characters?

Few women there be who can *love* a man for his intellect alone. When the complex of emotional reactions called love arises, it is, as a rule, stimulated by the various qualities which go to make up the *personality* as a whole—physical, emotional and mental. After one has been through the devastating psychic and physical traumas which this patient suffered, his personality may be radically altered—he may no longer be at all the *same man* the lady loved before he sailed overseas.

Most normal women have, in greater or less measure, two great biologic needs: to experience sexual gratification and to bear children. In some, one predominates, and, in others, the other. In the vast majority

of cases, the marriage which does not give a woman both of these experiences, leaves her with a more or less well-defined sense of vacuity and frustration. If either or both of these urges remains unsatisfied, it is probable that, sooner or later, she will give herself, openly or clandestinely, to a man who can fulfil these deep and elemental desires.

Endocrine therapy may be able to restore this man's appearance of masculinity and, perhaps, his *potentia coeundi*, but never his power of procreation. A normally-sexed woman might be able to live with him happily, if she had no keen longing for motherhood; but even then, the tenure of her happiness would be precarious, for, as yet, we have no sure means for the permanent restoration of masculine powers. If her "mother instinct" were strong, the time would surely come when she would feel defrauded of her birthright.

My first recommendation to this patient would be a full and free discussion of the whole matter with his fiancée, either they two alone or with my assistance in obtaining a full understanding of all the questions involved. That cause for anxiety would then be off his mind, one way or another.

The next step would be a frank consideration of just how important to his life work an appearance of masculinity might be. Being a physician, he would readily understand the possibilities of success and failure with gland transplantation and hormonal therapy, and the course to be pursued could be worked out between us.

Briefly, there should be a good prospect of restoring this man to a life of usefulness and reasonable happiness; but, in my opinion, marriage could never mean for him anything but a probability of psychic and professional wreck, leading to long misery or to suicide.

#### Solution by Dr. Max Thorek, Chicago

I am very glad that the discussion of this case has been rather full and very interesting. Dr. E. I. Raymond speaks of giving his patient "some reliable preparation of Leydig cells for the rest of his life". This brings us to consider the question of ophotherapy. At the present time ophotherapy has proven an absolute failure in my hands and, from a study of the literature, I find that the majority of serious workers in this field sustain my findings. The reason for this is that, in the preparation of an extract of the testicular substance, the process used for such preparation usually de-

stroys the active principle of the hormone. It is surprising to note that while the administration of ovarian extract by mouth very frequently gives the desired results, the administration of the testicular substance has not met with much success. Why this should be so is not at all clear, but it is, nevertheless, a fact. Stanley, who injects the whole testicular extract in a raw form, states that he is getting good results with it by subcutaneous administration. This seems to me to be a much more plausible way and should tend to give better results than the administration of the preparation of the male gonad by mouth.

Dr. Raymond suggests, however, that we use some form of the gonad preparation. The use of this in diabetic and senile patients is sound and his suggestion should be heeded. I am very pleased to note that the doctor speaks of restoring the mental balance in these cases, for it is a well-known fact that men who fear that they are growing impotent or who know that impotence has actually taken place, are prone to feel that their manhood and activity are being lost or are waning, and many forms of introspection and many psychotic states will appear. That this attitude is wrong is well-known, for it has been distinctly proven that performance of the sexual act is not at all a *sine qua non* to perfect physical and mental well-being. On the contrary, some men feel that the results from sexual hyperactivity are frequently a serious interference with their contribution to the fields in which they are engaged.

This thought directly brings me to consider the statement of Dr. J. F. Roemer, who aptly says that "the patient must be brought to see that sexual intercourse is not all there is to love and the married state." I advise all my readers to revert and study the splendid remarks submitted to our discussion of this condition by Dr. Roemer. I congratulate him on his philosophic thoughts. I agree fully with all he says. However, I want to emphasize that inasmuch as there is in the case under discussion a regression of the secondary sex characteristics, as shown by the change of voice and by the sparseness of the hair, it will be necessary, if psychotherapy is to be a success, to supplement it with something that will improve these conditions. I know no better method of alleviating these conditions than by a well-selected and properly performed transplantation of human testicular tissue into this individual. This will,

of course, if the transplant vascularizes, be followed by more or less success. A re-implantation may become necessary a little later, but so long as we can improve this unfortunate condition every effort should be bent to use psychic and physical means to restore this individual to as near a state of happiness as is humanly possible.

We next find ourselves face to face at the Round Table discussion with our distinguished friend and editor, Dr. George B. Lake. His scholarly dissertation contains some very sound reasoning, but there are some things which require modification. For instance, I am of the opinion that marital happiness depends upon the harmonious understanding of both the husband and the wife. I have seen many cases where the woman, following some pathologic condition, became incapable of serving her husband sexually. The man, whose love for his life partner was great, became psychically impotent and devoted his life to rendering his wife happy, and so lived in a state of celibacy. Conversely, I could cite a great many examples where the love of the woman was so intense, in similar cases, that her previous passionate nature yielded to absolute frigidity.

No iron clad rule can be laid down for every case. We all know that there are plenty of individuals who "cheat" regularly, and that there are a great many others aching for a chance to find justification in extramarital indulgence. The medical man cannot, however, consider the ideals of the question he is confronted with but must face the fact as to what is to be done to give the best satisfaction in every individual case. You can preach philosophy or any other form of verbal preaching to the hypersexed individual until doomsday, and he will not heed your admonitions. In our present case, a continuation of both methods, as agreed upon by all, will lead, I hope, to the desired result. I also believe that if the physician in charge of the case can render service only from a surgical and medical point of view and is not properly trained in psychotherapy, he should co-operate with a well trained psychotherapist and, by a combination of both methods, help the patient. Improvement, both somatic and mental, should be aimed at. I would add, however, that the women who can love a man for intellect alone are not few and far between; there are many, even as there are others who disregard his intellect entirely and live for sexual gratification only.

To sum up, let us agree, then, that some form of endocrine therapy be given our patient. In order of expectant success: (1) transplantation of human testes; (2) subcutaneous testicular implantation; (3) oopherotherapy by mouth.

**Problem No. 8 (Medical)**

Submitted by Dr. J. J. Bunn,  
Mt. Pleasant, N. C.

Patient a woman, 68 years old; has had high blood pressure (up to 250 mm., systolic) for a number of years; arteries not markedly sclerotic; very nervous temperament; several of her relatives have died of apoplexy; said to have had an attack similar to the one here reported about one year ago.

*Present Attack:* The patient complained of feeling faint and nauseated and vomited once. She did not fall, as she was in bed when the attack came on. In the afternoon she had received word of the death of her sister, with a diagnosis of cerebral apoplexy, but the news had not seemed to disturb her seriously.

I found her covered with a cold sweat; pulse rapid, weak and of low volume. She was restless and threw herself about in bed, remarking that she was going to die. She said she had no pain but "felt funny in the pit of the stomach". I did not take the temperature, but am sure it was below normal. The urine contained no albumin and had a specific gravity of 1010. Her bowels moved once, in the bed. There was no paralysis of the body or limbs. One dose of 3/8 grain (24 mgm.) of morphine was given, but it did not quiet her perceptibly.

She lived for about one hour and retained consciousness to the last. Shortly before her death she complained of pain in the lower part of the back. At the moment of death she threw up her hand and cried, "I am gone"; she then drew her lower eyelids down and, at the moment of her passing, the right corner of her mouth was awry.

An autopsy was not obtained.

*Requirements:* (1) What was the cause of death? (2) Why? (3) What, if any, treatment might have saved life?

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## Partial Payments for Medical Services

*The physician will be better off financially and every other way by the adoption of some policy which will permit some kind of a settlement of any and all accounts with his patients, even though it is made on the partial-payment plan, over a series of months or years. This plan has now been adopted extensively by a large class in the community. The partial payment plan for industrial workers is worthy of adoption on the part of physicians whose practice is not confined wholly to the well-to-do.—Editorial, J. Indiana M. Assn., Feb. 15, 1928.*



# Clinical Notes and Practical Suggestions

## Endocrine Factors in Arthritis

**G**ASTROINTESTINAL disorders and emotional disturbances, which upset the endocrine balance, *plow the ground* for arthropathies. Infected tonsils and teeth, alone, are not responsible for arthritis deformans, and too many of both these organs are needlessly removed, without first determining *exactly* what part they play in the condition of the particular patient affected.

The *posterior* nasal sinuses are important in these cases, but it is the *internist*, and not the rhinologist, who must decide just how important they are. The rhinologist can neither see nor transilluminate the *posterior* sinuses, and x-ray studies are unreliable. Clinical evidence must settle the question, and the patient's resistance is the main factor. In general, if *pus* flows the patient is reasonably safe. It is the cases with a thickened, spongy mucous membrane and *no discharge* that are dangerous.

Influenza is *epidemic sinusitis*; and hidden sinusitis is frequently the cause of the familiar "morning grouch." Diseased mediastinal lymph glands are a secondary condition and are also important.

Much of the etiologic background of arthritis is to be found in the *psychic life* of the individual, which, in turn, affects the *endocrines*. A careful study of the history, especially with regard to psychic traumas, is immensely helpful. I have known several cases where violent emotional experiences, of a negative type (such as fear and sorrow), have been promptly followed by the appearance of arthropathic symptoms. Sometimes an adjustment of the *social circumstances* of a patient, in regard to the domestic life, business or some other matter, will do more good than all other forms of treatment.

The bacterial flora of the gastrointestinal tract must not be overlooked nor underestimated. The "food sensitiveness" which is present in some of these cases will fre-

quently disappear if the bowel be flooded with *buttermilk* for one week.

*Hypertrophic* arthritis has a background of infection, as a rule, and yields to the clearing up of the infectious foci. These cases recover early, or not at all.

*Atrophic* arthritis is a much more difficult and complicated matter, but, by proper methods, a cure is possible in 47 percent of cases, and improvement in another 30 percent.

The first definite lesion is atrophy of cartilage; but, before this, *nervous* symptoms are present — pain, paresthesias, psychic instability, etc. Many patients have had their *spines* treated for "neuritis" when there were no signs of inflammation nor any provocation for such a condition.

A strong and healthy young man of 25 years was buried by the caving in of a gravel pit and was not extricated for some hours. After this tremendous *emotional strain* (without any anatomic lesions) he suffered for 9 months with easy fatigability and other symptoms of "neurasthenia," after which arthropathic symptoms appeared. He is now a cripple with arthritis deformans.

Whenever a severe psychic injury has occurred, the patient should be *put to bed* for a time, carefully fed and treated by *psychotherapy*. Such management will frequently prevent, not only arthritis, but also various other morbid conditions.

*Physical therapy*, if intelligently applied, is helpful, by relaxing spastic muscles and permitting proper *exercise* — not *walking*, but *calisthenics*, taken flat on the back, in bed.

Another measure which is of very great assistance in relaxing stiff joints and relieving pain (though I do not believe it should yet be considered as a positively curative agent), is the intravenous administration of *amiodoxyl benzoate*.

In arthritis it is especially necessary that we do not attempt simply to treat a disease.

\*Abstract (by G. B. L.) of paper, "Recent Studies in the Treatment of Arthritis," read before the Illinois State Medical Society, May 8, 1928.

but that we *study the patient* and adapt our therapy to his individual conditions.

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#### ACROMEGALY AND GENERAL CONSTITUTIONAL RETARDATION\*

*Case 1.*—It is possible to have acromegaly without any changes in the sella turcica or evidences of intracranial tumor. There is such a condition as hereditary, acromegalic constitution.

The case presented, however, was not of this type. The symptoms and signs have come on in the last 4 or 5 years. The patient presents, in mild degree, the typical leonine facies and enlargement of the extremities.

We may have here a simple hyperplasia—an acromegaloid condition—which requires no treatment; or the malady may progress and require treatment at a later date, by x-rays or surgery.

*Case 2.*—The patient gives the impression of an undeveloped boy. He is small in stature, the genitals are of the infantile type, there is no pubertal growth of the pubic and axillary hair and his demeanor is that of a boy of 11 or 12 years, though he is actually 18 years old.

There are several types of retarded growth. The condition may be constitutional, producing the primordial dwarf who is a miniature edition of an adult man; or the delayed development may be due to deficiency in the thyroid or pituitary secretion.

This patient is not a primordial dwarf, as he shows none of the physical signs of adulthood.

He is not a hypothyroid patient. There are no signs of *cretinism*. His face is that of a normal, good-looking boy and his intelligence corresponds with his appearance; his skin is smooth, clear and pliable; his tongue is of normal size and appearance.

In *hypopituitarism*, affecting the anterior lobe, there is atrophy of the testicles, a rather prematurely aged look to the face and no tendency to psychic infantilism.

The testicles, normally, do not increase in size between birth and the age of 10 or 11 years. This patient has testicles ap-

propriate to the latter age: They are not atrophied. His face looks boyish and his psychic life is that of a child.

A child differs from an adult in *every cell of his body*—not in the endocrines alone. This is a case of *general constitutional retardation*. He may develop, later, with or without treatment, but probably never to full adult standards.

Treatment with pituitary substance or by testicle grafts helps some cases, but not all.

G. B. L.

#### THE UNIGLANDULAR ORIGIN OF PLURIGLANDULAR SYNDROMES\*

We must push forward our studies of the functions of the glands of internal secretion, and in doing so we must remember that our researches may be carried out in the laboratory and also at the bedside, both types of work being indispensable to the progress of knowledge.

The secretion of each of the endocrine glands is *specific*, but the functions of all these glands are interrelated in a bewildering network of reciprocal relationships, so that it would appear as though all endocrine disorders must be pluriglandular in origin.

There are nine (9) glands of internal secretion, now recognized and accepted as such, and there are six (6) different forms of disturbed function which may affect any one or any combination of them—dysfunction (abnormal), hyperfunction (overactivity), hypofunction (lack of activity), dyshypofunction, etc. This gives us a possible variety of endocrinopathies represented by 9<sup>6</sup>, or 531,441.

Most endocrine disturbances, while showing one or more symptoms commonly associated with each of several of the different glands, present a preponderance of manifestations associated with one particular gland, and, if this organ, which overshadows the others in the clinical picture, can be put right, the symptoms referable to the other organs, which have been disturbed by its malfunctioning, will clear up at the same time.

In order to diagnose a true pluriglandular disease, one must be able to demonstrate that two or more of the endocrine organs are simultaneously and primarily involved. Such cases are very rare, there being but

\*Notes from a clinic by Prof. Julius Bauer, of Vienna, at Charity Hospital, New Orleans, La., March 6, 1928.

\*Abstract (by G. B. L.) of Presidential Address before the Association for the Study of Internal Secretions, Minneapolis, Minn., July 12, 1928.

12 to 15 authentic reports in the literature. A keen and accurate diagnosis points to the treatment indicated.

The development and progress of the sex life would seem, at first thought, to be the function of the gonads; but in *childhood myxedema* we see precocious puberty; while, if this change develops late and slowly, we are likely to find a pituitary disorder. If the thyroid or the pituitary is properly treated, the "gonad" symptoms will be readily controlled. Amenorrhea and exophthalmos—usually associated with thyroid disease—may be cause by *acromegaly*, and also by *hypofunction* of the pituitary. The balance is so nicely adjusted that any notable degree of disturbance, in either direction, may give rise to serious trouble.

A patient with primary deficiency of the secretion of the anterior lobe of the pituitary will have short legs; while primary ovarian disease will give rise to disproportionately long legs. We must study the bones of the patient by means of the x-ray. If his "bone-age" is decidedly greater than his chronologic age, it is decidedly probable that his adrenal cortex is involved.

A sudden amenorrhea, followed by the development of hirsuties, looks, at first, like an ovarian disorder; but is very likely to have its origin in the adrenal cortex. A study of well-made pyelograms will often show which suprarenal body is involved. We must remember that aberrations in the sex history are not always due to variations in gonadal function, and may be corrected by finding and treating the gland primarily involved.

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#### ENDOCRINE PRODUCTS IN OBSTETRICS AND GYNECOLOGY

Considering the vomiting of pregnancy from the endocrine standpoint, I wish to say that it occurs usually during the first three months; and investigators have discovered that the female sex hormone is not found in the blood before the twelfth week (placentation).

Gynecologically, the follicular hormone is the more active; the luteal less, hence the whole ovarian extract is of greater use, and I am sure this has applied equally well in my obstetric cases.

Novak, gynecologically, has gotten encouraging results in "mimic" administra-

tions; i.e., by giving a series of injections of the follicular substance of the ovary, and then a series of the luteal, this being better than either one alone.

More can be done if greater intelligence of application is acquired, and I intend to give organotherapy a more extensive test, for I am certain that many of my failures from this standpoint, both gynecologically and obstetrically, have been due to:

- 1.—Lack of sufficient attention.
- 2.—Inefficiency of many of the glandular products.
- 3.—Administration of the wrong product, or lack of proper combinations.

I have administered these preparations by mouth or intramuscularly. Ovarian extract has been of use to me for pernicious vomiting of pregnancy, but the luteal extract has always failed me. Vogt quotes Hofbauer as finding that insulin (as the pancreatic hormone) and ovarian preparation (whole ovary) equilibrate hypofunction of the ovary and cause recession of hyperemesis.

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#### ENDOCRINE EPILEPSY

Dr. J. Montgomery Anderson takes a step in the right direction when he speaks of "endocrine epilepsy," in the December number of *CLINICAL MEDICINE AND SURGERY*. I want to take one step further and say that *all* genuine epilepsy is endocrine. After over twenty-five years of study of the disorder, I want to give the following as a definition of epilepsy:

An epileptic is a person who has a low percentage of colloid calcium in the blood; who has a "spasm temperament" that will respond with a spasm on almost any form of irritation in the system; and all that I have encountered are hearty meat eaters.

The parathyroids control the level of calcium in the blood. If they do not secrete a normal amount, the lime level is low and various results follow. The parathyroids also destroy two of the amino-acids of meat which, if not destroyed, become poisons and consequently irritants in the system—guanidine and adenine.

If large amounts of meat are eaten and the two amino-acids are unchanged, or only partly changed, they become irritants and I have denominated this as *primary irritation*, because it is always present. Constitu-

pation, intestinal parasites and a long list of other disturbances I have called secondary irritants, for the reason that we may find only one of them present in a number of epileptics in a community.

I used to hear it said that epilepsy was hereditary. What is hereditary in this case? My study of epilepsy in several families caused me to conclude that it is not the spasm condition but the low percentage of calcium in the blood, as a result of which I noted three conditions: The "spasm temperament," the "suppurating temperament" and what I have called the "cry-baby" temperament. The first needs no explanation. The second is a condition in which any kind of abrasion of the skin leads to suppuration. Look at the faces of a room full of school children. There will be several with sores about the mouth, and a little questioning will show that these children have sores that do not heal readily on other parts of their bodies.

For the third I will describe a case. One evening as I was sitting on my porch a young lady passed, crying as if badly hurt. I followed her a short distance, to ascertain the cause of her distress and found that she was just having her "evening cry." A few days later a four year old girl was brought to me who had similar crying spells without any evident cause. Later I found another child here, and in another town I found a married woman with two children who had the same condition.

What was the hereditary factor in these cases? Of the two children of the last mentioned woman, one is an epileptic and the other is a diabetic. (Is diabetes mellitus due to a low blood calcium percentage, also?) In another family, the father has a low calcium level; the son is (or was) an epileptic; the oldest daughter showed the "suppurating temperament"; and the youngest girl was a "crybaby." In still another family, the father shows the "suppurating temperament"; one daughter is an epileptic; and a grand-daughter is subject to suppuration. I found recently one case that was both suppurating and "crybaby." It seems to me that the inherited factor is the blood calcium level, rather than the temperament.

#### Treatment

The only restriction I make on the diet is to eliminate meat from the menu. This enables the patient to eat with the family

without embarrassment, if strangers happen to be present.

If the vitality is low, treatment with triple arsenates with nuclein will correct that condition.

To raise the blood calcium level, parathyroid substance, 1/10 grain, three times a day should be given. If it seems necessary, four doses a day may be given for a few days. Thyroid substance, 1/3 grain, given with the parathyroid, helps elimination and sedates any possible exciting effect the parathyroid may have on the gonads, as the two are in different endocrine chains—the parathyroid and the gonads in the parasympathetic chain and the thyroid in the sympathetic.

In the case of a child, it may not be necessary to give three doses a day for more than a week, then two a day and finally one. But in the case of a person who is past middle life, where the glands of internal secretion have begun to regress, it may be necessary to continue one dose a day for some time to maintain a proper calcium level in the blood. If the person has been taking bromides for some time the attacks will gradually stop; in the case of luminal, when that is stopped there will be one or more spasms at the start.

All the "suppurating temperament" needs is a few treatments with parathyroid, repeated occasionally if the symptoms return.

Treat the "crybaby" as an epileptic until the attacks cease, and then give a few doses of parathyroid if a nervous condition returns later. With a little care of all three forms, in children, the patients may grow up healthy.

Our last case was one of premature development in a boy, now 12 years old. Unless these children have the "spasm temperament" their premature development is not noticed. In the case of girls, the first menstruation is ushered in with one or more severe spasms. This boy was mature at 10 years. It was noticed that when asked a question at school he would put his hand to his head as though thinking. Later he would have spells of "blowing," followed by protruding the tongue at one side, drumming and rubbing his hands together. He also showed sexual erethism (how long it had been present I do not know), which was very marked when I saw him. He had stoop shoulders, a flat chest, flabby muscles and other evidences of low vitality. I saw him have one fainting spell but he did not

fall: The true spasms were evidently approaching.

This boy was given triple arsenates with nuclein (Abbott), parathyroid, gr. 1/10, and thyroid, gr. 1/3, three times a day, with instructions to eliminate meat from the diet. After about a month of this treatment his mother wrote, saying that the boy was so much better that he was in school.

G. B. FRENCH, A.M.

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#### FAIRY TALES OF PROCTOLOGY

"Digitally Speaking"

In the days of not so long ago there were, throughout the country, many merchant guilds among the men of business. Of them all, the shrewdest and, indeed, the most consistently successful was a group who called themselves "Insurance Companies". These were formed by some of the wisest men in the land and, for a stipulated sum, they would cheer you up to the extent of betting that you would be alive ten, fifteen, twenty or so many years hence. Of course, the charity in the affair stopped right there and henceforth the matter became one of shrewd business. Every effort was extended to pick out only sure bets.

As clever business men they employed doctors equal, in skill of diagnosis, to many of the best physicians throughout the land. These doctors were called examiners and they made a thorough inspection of the body of the party to be bet upon; an inspection, incidentally, which carried them from the soles of the feet to the roof of the skull.

But, as is often the truth in both investigations and discussions, the principal and important matter is neither at one extreme nor the other. However, these examiners were no half-way men and, in their rapid survey of the aforesaid body, scurried from head to foot. The idea of a rectal examination, if it occurred at all, was hastily hurdled.

This was all in accordance with the medical soothsayers of the times and forsooth they spoke as follows:

"Making a rectal examination is *so* unnecessary and, in general, *so* inconvenient that the best policy is usually one of excommunication insofar as the lower end of the gastro intestinal tract is concerned, if one *must* appear thorough, which at times is distressingly so, then it is only neces-

sary, as a matter of form, to slip a rubber glove on and thrust the finger—the 'educated finger'—into the rectal cavity. Be sure to thrust the tip of the finger, wherein lies the tactile sense, well past the anal canal. In this way about eighty percent of ano-rectal lesions may be avoided and, since the tip of the finger can not reach the recto-sigmoid junction, where the other eighteen percent lie, a perfect score may be maintained. Exploration of the rectum with rectoscopes and other instruments takes the romance out of rectal examinations and reduces the matter to prosaic terms of accuracy. Ulcers may be seen, polyps and early cancerous conditions discovered and, in short, one is deprived of the comfort that comes from learning by simple digital examination that 'the rectum is negative'".

So it came to happen that, digitally speaking, the case was negative in all respects—but the patient died some months later from a carcinoma of the rectum. Now, this in itself is not a strange event, since the situation has many times presented itself before that, and perhaps once or twice thereafter. Of course, in these modern days it is rather difficult to understand just how such a thing could happen. But it *did* happen, or at least the patient was buried under the impression that it had happened, and the case was so recorded; and thereby hangs the tale, *digitally speaking!*

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#### GASTROINTESTINAL AUTOINTOXICATION IN NERVOUS DISORDERS\*

Indican is not poisonous, but it is an *index* of the amount of various poisonous substances which may be present in the blood and tissue fluids. A person may, however, suffer from intestinal autotoxemia without showing indican in the urine.

The functions of the mind are probably altered, especially in those whose psychic centers are below par, by the long-continued presence in the blood of mildly toxic substances. In patients suffering from intestinal toxemia, sleep is not refreshing and headache is frequent. These people tire easily, wake up tired and feel better later in the day.

The cerebrospinal fluid probably has a triple function: mechanical protection of

\*Abstract, (by G. B. L.) of a lecture before the Interstate Postgraduate Medical Association, Oct. 20, 1927.

delicate structures; the carrying of nutrient material; and the removal of wastes.

The mechanical function is important. It equalizes changes in arterial pressure. Toxins may affect the pressure of the cerebrospinal fluid; and neurasthenics frequently show irregularities of blood pressure. If we can correct these, improvement is likely to follow.

The symptoms of neurasthenia resemble those produced by conditions of organic origin, especially senescence, and it is highly probable that many of the symptoms are produced by changes in the pressure of the blood and cerebrospinal fluid, hypotension causing the characteristic depression.

In these patients, vertical and occipital headaches are common, and are relieved by lying down. Healthy persons will have similar headaches as a result of physical or mental strain or fatigue.

*Treatment:* The earlier we treat these patients, the better the prognosis. The tissues seem to acquire a *morbid habit* if poisoned for long periods of time.

*Digitalis* is the best drug when the blood pressure is low; periodic *phlebotomy* when it is high.

Search carefully for signs of intestinal autointoxication and, if it is demonstrated, give *urotropin* (*methenamin*) for its relief.

OTTO J. KAUFMANN, M.D.,  
Professor of Medicine,  
University of Birmingham, England.

#### CHLORAZENE IN AUTOTOXEMIA

So many cases of "rheumatism" and other conditions of general ill-feeling and incapacity result from intestinal intoxication that a remedy for this condition should be welcomed.

My method of dealing with such cases is as follows:

Make up a number of capsules, each containing 2 grains of Aromatic Chlorazene powder, thoroughly mixed with 2 grains of powdered charcoal.

For the first three days, give one tablet of calomel, podophyllin and bilein compound (calomel, 1/6 grain; podophyllin, 1/6 grain; bilein, 1/8 grain; strychnine arsenate, 1/250 grain) at bedtime, and one of the capsules half an hour before breakfast, followed by a glassful or more of water. After three days, give the capsules night and morning, always followed by plenty of water.

The calomel, podophyllin and bilein tablets may well replace the capsules, at night, for three days out of each week. Two weeks of this treatment is generally enough to make the patient feel well, and the results last for two or three months, after which the treatment may be repeated.

This medication, if used in the spring and fall, seems to raise the resistance of the patients who take it, so they are less susceptible to "colds" and bronchitis.

WILLIAM C. FREEMAN, M.D.,  
Dallas, Tex.

[The giving of Chlorazene (chloramine) by mouth may seem unusual to some, but it is not a wholly new and untried procedure. In the January, 1925, issue of CLINICAL MEDICINE (page 49), Dr. C. H. Woolgar recommended its oral use in the treatment of dysentery; and in the June, 1928, CLIN. MED. AND SURG. (p. 422) Dr. Israel suggested it as a remedy in pulmonary tuberculosis. There are other such references in the literature.

It would seem that this treatment deserves a more extended trial, and we shall be glad to publish the experiences of any of our readers who experiment with it.—ED.]

#### DEXTROSE, INTRAVENOUSLY, IN EPIDEMIC ENCEPHALITIS\*

Intravenous injections of glucose (dextrose) solutions have given good results in cases of epidemic encephalitis. Of 40 cases so treated, 22 were entirely relieved, 12 were somewhat relieved and 6 experienced no relief.

Injections of a 10-percent solution of dextrose, from 150 to 500 cc., were given daily for 15 or more days. The solutions must be freshly prepared. Old or resterilized solutions cause reactions.

It is difficult to make a diagnosis and we must be careful not to call obscure cases encephalitis.

Hyoscine hydrobromide helps the later Parkinsonian syndrome.

Autogenous serums are of value in some cases.

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\*Abstract (by G. B. L.) of a paper read before the Southern Medical Association, Nov. 16, 1927.

# Diagnostic Pointers

## EXCESSIVE JOY AND THE ENDOCRINES

Intense emotion—excessive joy or happiness—may overstimulate the endocrine glands and cause hypersecretion. Intense joy has been known to cause the onset of exophthalmic goiter.

Intense emotions are more likely to affect the adrenals than other glands; adrenalin raises the blood pressure and increases the blood supply to certain organs.—E. PODOLSKY, in *Pract. Med.*, Oct., 1925.

## MYXEDEMA AND PERNICIOUS ANEMIA

Many cases of myxedema show blood findings very similar to those seen in pernicious anemia. These yield promptly to the administration of thyroid extract.—DR. CHARLES T. STONE, of Galveston, Tex.

## TUBERCULOSIS AND HYPERTHYROIDISM

In tuberculosis, afternoon fever is a prominent symptom; this is not the case in hyperthyroidism.

In exophthalmic goiter the basal metabolic rate is constantly high; this is not so in tuberculosis, in the afebrile periods.—DR. C. A. MCKINLAY, in *Journ.-Lancet*, June, 1927.

## ABORTION DUE TO HYPOTHYROIDISM

Thyroid insufficiency may be responsible for repeated abortions. Such cases have been seen which made no response to antisiphilitic treatment, but where the patients carried children to term under thyroid medication.—DR. VIGNES, in *Progrès Méd.*, Aug. 13, 1927.

## ADDISON'S DISEASE WITHOUT PIGMENTATION

Addison's disease may be present without the bronzing of the skin which is considered characteristic.

Clinical diagnosis is made upon the progressive and appalling loss of strength and vital energy, low blood pressure—down to 60 mm., systolic—and the gradual failure

of the life processes—pulse, temperature, metabolism, renal functions, etc. It is confirmed by finding tuberculosis of the suprarenal glands at autopsy.—DRS. D. G. GHRIST and L. G. ROWNTREE, of Mayo Clinic, in *Endocrinology*, Nov.-Dec., 1927.

## ANAPHYLAXIS AND THE ENDOCRINES

Epinephrin, pituitary extract and parathyroid, given at the proper time, in correct dosage can prevent anaphylactic phenomena.

Thyroid extract and insulin increase the sensitiveness of guinea-pigs.—DR. K. HAJOS in *Klin. Wchnschr.* 5:1393, 1926.

## THE SKIN AN ENDOCRINE ORGAN

Certain recently discovered functions of the skin suggest that it may prove to be an endocrine organ, and Bloch has given the name "dermin" to its hypothetic hormone.

Extracts of the subcutaneous cellular structures of certain turtles, when administered to human beings, have caused evidences of dermal regeneration, with tightening of the skin and the disappearance of cutaneous blemishes.—DR. CURT THOMALLA, in *M. J. & Record*, Feb. 1, 1928.

## LIVER THERAPY AND LEUKOCYTES

Liver treatment, besides altering the blood formula in pernicious anemia, appears to have a definite affect on the leukopenia which is generally present with this condition.

Liver diet seems to stimulate the production of leukocytes so that leukopenia is abolished.

Eosinophilia appears to be a part of the patient's reaction, and the appearance of eosinophiles is a favorable prognostic sign.—DR. L. E. H. WHITBY, in *Lancet*, Feb. 11, 1928.

## ENDOCRINE THERAPY SPECIFIC

Endocrine therapy is *specific medication*. One can no more cure a pituitary deficiency by giving gonad extract than one can cure syphilis by giving quinine.—DR. JAMES H. HUTTON, in *Illinois M. J.*, Feb., 1928.

# Thumbnail Therapeutics

## PARATHYROID THERAPY

An active crystalline extract of the parathyroid glands, soluble in water, has been found useful in the treatment of various forms of tetany and spasmophilia, acute and chronic parathyroid insufficiency, tuberculosis, gastric ulcer, psychoneurosis associated with parathyroid insufficiency and exophthalmic goiter. The greatest indications for it is the production of relative or absolute hypercalcemia.—DR. LOUIS BERMAN, *M. J. & Rec.*, August 3, 1927.

## DEAFNESS AND THE ENDOCRINES

Intestinal focal infection may be a factor in the etiology of progressive deafness, and should be corrected.

In addition, thyroid extract should be given in the smallest effective dose—usually  $\frac{1}{2}$  to 1 grain (32 to 64 mgm.) to adults and  $\frac{1}{4}$  grain (16 mgm.) to children, at bedtime. The dosage should be reduced in the summer and during menstruation.—DR. HUNT, in *Med. Times*, Aug., 1927.

## THYROID EXTRACT IN SCLERODERMA

Cases of scleroderma are often benefited by the use of thyroid extract, particularly when fairly large areas are involved.—*Urol. & Cutan. Rev.*, Oct., 1927.

## TESTICULAR EXTRACT IN POST-CLIMACTERIC PRURITUS

In cases of pruritus, in women, occurring after the menopause, much relief has been obtained following subcutaneous or intramuscular injections of testicular extract. Two or three injections were given.

Testicular extracts produce good effects in women whose vagus and sympathetic systems are disturbed.—DRS. GALLERAUD and MEYER in *Fortschr. d. Med.*, Feb. 18, 1927, (*Endocrine Survey*, Feb., 1928).

## ENDOCRINE DEFICIENCIES AND INTESTINAL AUTOTOXEMIA

Certain cases of ovarian insufficiency, with menstrual and general disorders, may be due to intestinal toxemia and liver insufficiency, even when constipation is not a marked feature of the case, and can be

relieved by the elimination of all foci of infection (especially that in the bowels), together with a general detoxicating and eliminant treatment and the exclusion from the diet of animal and vegetable purins.—DRS. M. J. BARILARI and M. MARGULIS, in *Semana Méd.*, Dec. 22, 1927.

## SKIN REACTIONS AT THE MENOPAUSE

The most common skin manifestations observed at the menopause are: rosacea (both of the erythematous and pustular types), pruritus, eczematous reactions and alopecia areata.

The treatment consists in substituting the deficient ovarian secretion, with which thyroid extract may be combined.—DR. H. MONTLAUR, in *Paris méd.*, Jan. 21, 1928.

## GONADS VS. ADRENALS

Ovarian extract lowers blood pressure and dilates the vessels. Testicular and ovarian extracts may be regarded as the antagonists of epinephrin in relation to this action.—DRS. M. KAMENEV and N. MANZ, in *Trudy. Ukrain. Psichonerv. ceskogo. Inst.* 4:19, 1927.

## ESOPHAGEAL AND URETHRAL SYMPTOMS IN MYXEDEMA

In a case of myxedema in an adult 58 years old, showing esophageal and urethral obstruction, the administration of 2 grains (0.13 Gm.) of desiccated thyroid substance, daily, caused disappearance of the esophageal and urethral troubles after three weeks. DR. H. H. RIECKER, Ann Arbor, Mich., in *J. Michigan M. Soc.*, Feb., 1928.

## PANCREATIC EXTRACT IN MALIGNANT DISEASE

The administration of an extract of sheep pancreas has been found to cause immediate symptomatic improvement in patients with hopeless malignant disease. It also seemed to have some effect on the disease itself. The pancreatic extract may be given orally or injected. Also fresh gland substance may be given as part of the diet.—DR. A. H. MAY, Buffalo, N. Y., in *M. J. & Record*, Feb. 1, 1928.

# Current Medical Literature

## PHYSICAL THERAPY AND THE ENDOCRINES

In *Arch. Phys. Therap. X-Ray, Radium*, May, 1928, Dr. Jas. H. Hutton, Chicago, states his opinion that the popular belief that Graves' disease or primary exophthalmic goiter is due to hyperfunction of the thyroid is incorrect, and that the real basis of the disease is probably in the adrenals. The partial destruction of the thyroid, either by surgery or radiation, based on this theory is also incorrect; but radiation has the advantage over surgery that it does not permanently cripple the gland and eventually it can resume its function more or less normally.

In view of the increasing doubt in regard to the true etiology of Graves' disease and toxic goiter, it would seem that common sense conservatism should dictate that treatment which subjects the patient to the smallest risk. On this basis medical treatment and physical therapy should handle most of these cases.

The theory that destroying the ovarian function will cause a retrogression of fibroids of the uterus is not correct, as shown by the fact that the menopause, with its partial cessation of ovarian function, does not necessarily check the growth of these structures.

Where ovaries are radiated, Dr. Hutton is of the opinion that any good influence that such treatment may have on fibroids is due to incidental raying of the tumors themselves. He further thinks that the pituitary has more to do with these growths than has the ovary.

## THYROID THERAPY IN SKIN DISEASES

Thyroid may be given in three groups of skin diseases: (1) where there is definite evidence of subactivity of the gland, as in the xeroderma of myxedema; (2) where there is no evidence of such subactivity, but where the effects of thyroid therapy may be expected to remove the causes or relieve the results of the skin disability, as in certain cases of chilblains; (3) diseases due to some obscure disorder of metabolism, calling for a general increase of vital processes, such as chronic urticaria.

The dosage depends on the age, weight, and condition of the patient, and the degree, if any, of hypothyroidism present. An adult with slight myxedema may begin with three grains of dry thyroid daily; an adult showing no evidence of glandular deficiency can take  $1\frac{1}{2}$  grains daily without danger. The dose is very slowly increased at monthly intervals. In patients who are sensitive to thyroid medication the dose must be re-

duced; sometimes a very minute dose will improve the skin condition without producing any discomfort.—DR. P. B. MUMFORD, in *Lancet* (London), Oct. 22, 1927.

## IMPLANTS OF SHEEP TESTICLES IN HUMAN SUBJECTS

After a study of four years and the experience of 50 cases, Dr. G. R. Satterlee, New York, in *M. J. & Record*, Feb. 1, 1928, states that the subcutaneous injection of macerated sheep testicles, in both men and women, causes:

- 1.—Marked and sustained improvement in physical condition, in some cases of diabetes.
- 2.—Sustained improvement in urinary glucose in some of these cases.
- 3.—Generally increased vigor in nearly all cases.
- 4.—Improved circulation in the skin and alimentary tract.
- 5.—Absence of all harmful results.
- 6.—Certain definite improvement in the blood picture.

The injection is made with a good-sized syringe, through a large-calibered needle. If 3 or 4 Gm. of the macerated substance are injected in divided doses of 1 Gm. each, in the deep subcutaneous tissues, preferably of the abdomen, but little disturbance is experienced. Occasionally coagulation necrosis takes place, but there have been no pyogenic abscesses.

## HYPERTHYROIDISM AND MENTAL DEPRESSION

In *Allgemeine Zeitschr. f. Psych.* 83:296, 1926, Dr. Werwath reports that a woman, aged 44, with classic symptoms of exophthalmic goiter, had been suffering for seventeen years from severe attacks of depression. These depressive states finally became so severe that the patient had to be placed in an institution for a time.

Following thyroidectomy, the symptoms of depression gradually disappeared.

On the basis of experiences in three analogous cases, a connection between Basedow's disease and manic-depressive psychosis is assumed, and possibly a toxic (thyrogenous) element.

## ORCHIC EXTRACTS

Formerly, the difficulties in the administration of orchic extracts were that they were comparatively ineffectual by mouth, and too insoluble for injection.

In the *Practitioner* for December, 1927, Dr. E. Curnow Plummer remarks that we

now have soluble orchic extracts which can be given hypodermically, in doses of 1 cc., twice weekly. Their use is followed by an increase in mental and physical energy and in the sense of well-being; sometimes by augmented sex desire and power.

The effect of these injections is, of course, rather transitory, but as they are painless and without danger they can be repeated as long as necessary. There is a possibility that, by resting the testicles, they may recuperate and resume their functions.

#### INSULIN IN OVARIAN MENORRHAGIA

It is known that insulin injections produce temporary sterility in the female, but the mechanism of the action is not agreed upon.

Dr. G. Cotte, of Lyon, in *Presse méd.*, Feb. 11, 1928, refers to the recent discovery by Vogt that insulin diminished the duration and abundance of the menses in normal non-diabetic women. Vogt applied this finding clinically in 50 cases of ovarian menorrhagia, with most excellent results. He administered from 40 to 50 insulin units, in 2 injected doses, daily, starting from the fourth day of the menses.

Cotte applied Vogt's treatment in 4 cases of ovarian menorrhagia and also obtained most excellent results.

Insulin is of no use in hemorrhages originating from any other cause than ovarian dysfunction.

#### SOLAR RADIATION, THE PARATHYROIDS AND GROWTH

It is known that parathyroid hyperplasia occurs in animals kept upon a calcium diet. The same effect might be assumed in the absence of vitamin D.

In *Proc. of Staff Meeting of the Mayo Clinic*, March 7, 1928, Drs. G. H. Higgins and C. Sheard state that, as a result of experiments on chicks to determine the vitamin D energizing effects of solar radiations of various lengths, it was found that parathyroid hyperplasia ensues in chicks in the absence of the lesser wave lengths of sunlight; also that such hyperplasia is partially prevented by the addition of a small portion of cod-liver oil to the diet. In chicks, exposed to blue or amber light and maintained upon a diet without cod-liver oil, the parathyroids, at the end of one month, were nine times the size of the glands in a chick grown under vitaglass on the same diet.

The same authors' experimental investigations in regard to solar energy and growth showed that normal growth and development are dependent upon both the ultraviolet and the visible portions of solar radiation, all other factors remaining constant, so far as known.

The authors found, from experimental data on the quality and quantity of energy in solar radiation transmitted by various filters, and calculations made therefrom, that an energy equivalent of the short or

socalled vital rays (290 to 320 millimicrons) of 0.045 gram-calorie per square centimeter per minute, is ample to produce normal development.

#### PARA-THOR-MONE IN INFANTILE TETANY

"Para-Thor-Mone" is a standardized preparation of parathyroid gland, the potency of which is indicated in units as "one hundredth of the amounts of extract which will produce an average increase of 5 mg. in the blood serum calcium of normal dogs of approximately 20 kilos weight over a period of 15 hours."

"Para-Thor-Mone" was administered in 8 cases of infantile tetany by Dr. D. B. Leitch, of Alberta, Canada. In *Canad. M. A. J.*, Nov., 1927, he states that the use of the preparation increases the serum calcium and exerts a beneficial effect in infantile tetany. The dosage is usually 2 cc., subcutaneously, for about 4 days.

#### EPHEDRINE-NOVOCAIN (PROCAINE) ANESTHESIA IN THYROIDECTOMY

In *J. M. Soc. New Jersey*, Nov., 1927, Dr. G. P. Pitkin refers to the dangers of ether, gas and ethylene in thyroidectomy.

As an anesthetic, novacaine (procaine) alone cannot be relied upon for more than 15 to 20 minutes, which is frequently far too short a time for executing the operation; but with the addition of 1 cc. of a 3-percent solution of ephedrine, to 200 cc. of a 1-percent solution of procaine, anesthesia may be maintained satisfactorily for one hour.

In innumerable cases the author has found this not to vary 5 minutes one way or the other. The method does not produce shock, slows rather than stimulates the heart and does not impair respiration nor affect metabolism. There is no vomiting nor dehydration and there are other advantages over inhalation anesthesia.

The mixture of ephedrine and procaine does not deteriorate.

#### CHILDHOOD MYXEDEMA

Dr. Murray B. Gordon, Brooklyn, N. Y., in *Am. Med.*, Jan., 1928, classifies childhood myxedema as including the congenital, infantile and juvenile types.

Congenital myxedema has as its basis complete absence of the thyroid gland. The infantile type includes those cases in which the pathologic disturbance in the thyroid gland originated before birth, although enough thyroid tissue persists to enable the child to develop, but not along normal lines. Juvenile myxedema is the term applied when the condition develops as the result of an acute infection or nutritional disturbance, the thyroid gland being normal at birth.

While heredity may be a factor in childhood myxedema, it is difficult to estimate its influence.

The total energy requirements in childhood myxedema are 18 to 25 percent below normal, as shown both by Du Bois and Talbot; it may occasionally be even 50 percent below normal.

Diagnosis of childhood myxedema is fairly easy, but the condition may be confused with minor types of hypothyroidism, mongolian idiocy, endemic cretinism and other conditions due to dyscrasia of other endocrine glands.

The treatment of childhood myxedema consists in the administration of thyroid extract. Thyroid grafting is rarely used. Until some method of standardization is reached it is advisable to decide upon some certain manufacturer's product of extract and to continue to prescribe it by name. Treatment at the endocrine clinic of the Long Island College Hospital consists of starting with a very small dose and then gradually increasing it, at first twice a day, then three times daily. The first dose is 1/10-grain (.0064 Gm.) of thyroid extract, the next 1/8 gr. (.0081 Gm.), 1/4 gr. (.016 Gm.) and so on until one grain (.065 Gm.) of thyroid extract, three times a day, is reached, provided there is no undue reaction. During alternate weeks no medication is given. Improvement is checked by the basal metabolism. Treatment may have to be continued for many years.

#### THE FEMALE SEX HORMONE

O. O. Fellner, in *Zentralbl. f. Gynaek.*, Dec. 17, 1927, says that the occurrence of the female sex hormone in so many glandular organs is striking. It was found in the interstitial cells of the ovary, the corpus luteum, placenta, testis, decidua, thymus, prostate, in the urine, and, in slight amount, in the suprarenal cortex.

The female sex hormone is, nevertheless, a specific hormone, since it develops definite effects following administration, which other substances cannot incite.

The female sex hormone was encountered in embryos and in semen. Fellner found it also in hens' eggs, roe, flour and rice. There are probably functions still unknown which this hormone fulfills.

#### IMMUNIZING FUNCTION OF THE TONSILS

According to the researches of Dr. F. Pearce Strum, Lancashire, Eng., published in *Am. Med.*, Feb., 1928, tonsillar hypertrophy may be an attempt of the organism to make simple lymph organs perform the work of complex endocrine glands which are functionally incompetent.

Tonsillar hypertrophy constantly occurs at a time when the human being is not yet immunized; when infection is therefore most dangerous. Once immunization is effected,

both the pharyngeal and faucial tonsils normally tend to regress and disappear.

Tonsillar hypertrophy consists chiefly in an increase in the number and size of germ-cells; in infective conditions there is evidence that leukocytes, laden with captured microorganisms, come to the germ-centers for destruction. At least one, if not the only, function of the germ-centers is the manufacture of antitoxins and immunizing bodies generally.

The author cites several cases of children in whom deprivation of the pharyngeal lymph ring seemed to have been hurtful in effect, as removing a means of protection.

The theory of the protective role of the tonsil is, not only the most reasonable one, but also it is the only one which can be supported by clinical evidence.

#### ETIOLOGY OF DIABETES MELLITUS

In *Arch. Int. Med.*, October, 1927, Drs. J. Friedenwald and T. H. Morrison sum up the results of their investigations regarding diabetes mellitus as follows:

1.—There has been a marked increase in death rate and incidence of diabetes in recent years.

2.—The increase in the incidence of this disease, while it has included persons of all ages, has revealed itself most markedly in women at all ages and in men over 45.

3.—The incidence of diabetes is proportionately much greater among the Jewish race. This susceptibility has been variously estimated as being from two to four times as frequent as among the rest of the population.

4.—The cause of the greater susceptibility to this disease has as yet not been altogether satisfactorily established. Among the more frequent explanations given are: lack of proper physical exercise, unsuitable dietary habits, undue nervous strain and marked tendency to obesity, following the forty-fifth year of life. Without doubt, obesity plays by far the most important role. In this connection, Joslin has called attention to the important fact that the major number of causal factors referred to can actually be explained on the basis of obesity.

5.—The relation of obesity to diabetes becomes more evident in the study of blood-sugar tolerance curves in obese persons. In 57 percent of Paullin's cases, a lowered blood-sugar tolerance was noted, and the proportion was 68 percent in our obese Jewish patients. A certain number of these cases were detected in persons with early cases of diabetes. The variations between Paullin's and our own figures may perhaps be emphasized as further evidence in favor of the theory that there is a greater tendency to diabetes in obese Jews than in persons who are not Jews.

6.—The increase in the consumption of sugar during the past years has been assumed to be a factor in the production of obesity and, therefore, of diabetes. There is no evidence, however, to prove that the

overuse of sugar alone tends to produce this condition. Obesity can be produced as readily by the inordinate use of carbohydrates, fats or alcohol. It is likely that the overuse of foods in general, together with lack of proper exercise, has been the most important cause of obesity, and consequently a direct factor favoring the development of diabetes.

7.—Finally, as a result of these observations, it is apparent that in order to lessen the incidence of diabetes, the dietary habits of persons with a tendency toward obesity should be regulated, and adequate exercise should be instituted. This is especially important in persons past 45, and even more important among the Jewish population.

#### THE THYMUS IN CHILDHOOD

The general consensus of opinion today is that the thymus cannot be considered as an internal secretory gland, but is to be classed with the lymphoid organs and is perhaps associated with nuclein metabolism.

In *Northwest Med.*, April, 1928, Dr. B. E. Bonar, Salt Lake City, says that, in the new-born thymic enlargement is found in 40 percent, but such enlargement is not symptom-producing in this number. Increase of thickness anteroposteriorly is of much more importance clinically than is increase in other directions, on account of pressure symptoms, especially tracheal.

The cardinal symptoms of thymic enlargement are dyspnea and stridor.

X-ray examination affords the most information about the size of the thymus. Shadows extending beyond the vertebral transverse processes are usually considered enlarged. The thymic shadow includes that made by the great vessels and paratracheal glands, and when the latter are enlarged confusion may occur. There is one factor that must be considered: with expiration there is an increase in size of the shadow, while with inspiration there is a decrease. This is probably due to pressure on the thymus.

If x-ray evidence is negative, the result should not be considered final, in the presence of clinical symptoms.

X-ray therapy is the treatment of choice. Treatments are usually given one week to ten days apart, until the shadow has decreased in density rather than in size. Reduction in size is usually obtained with from three to six doses.

#### CLINICAL ASPECTS OF THE FEMALE SEX HORMONE

Dr. B. C. Hirst, in *Am. J. Obst. and Gynec.*, Jan., 1928, states that, for the normal performance of their cyclic functions, the female sex organs depend on a hormone secreted first by the theca cells of the graafian follicle, of connective tissue origin, and next by the epithelial cells of the granulosa, as the theca cells atrophy. The

hormone is present in greatest concentration and potency in the development stage of corpus luteum growth, and is entirely absent in its retrograde stage, in the non-pregnant female; it is also produced during pregnancy, but is then found in parts of the ovary from which it is absent in non-pregnant females; it is found in the blood stream in varying amounts during the menstrual cycle—most during the premenstrual congestion and least during the flow.

The female sex hormone, of all the endocrine and glandular secretions of the body, will induce estrus in a spayed animal. The hormone of the anterior lobe of the pituitary will not induce estrus; it can bring about an increased secretion of the sex hormone but it has no effect on a spayed animal.

The sex hormone, when administered by mouth, is positive in its action. But, judged in terms of mouse units, the tablets on the market are entirely insufficient in their content of sex hormone. Hirst, however, says that we are promised the production of a product for hypodermic injection which should give such results as have never before been obtained.

The generally uncertain and poor clinical results obtained, up to the present, must be attributed to the inadequate dosage compared to the weight, as contrasted with effective doses in experimental rodents. With the improved product and massive doses, physiologic results should, in future, be obtained rapidly. At present, Hirst has 4 patients under treatment with 25 to 100 rat units of sex hormone as the initial dose.

#### ENDOCRINE TREATMENT AND THE GENERAL PRACTITIONER

Dr. Abraham A. Levy, New York, in *Am. Med.*, Jan., 1928, offers some interesting remarks based on experience regarding the oral administration of endocrine medicaments.

Of the many preparations in use, whole gland extracts, and particularly the glycerin extracts, have proved more generally satisfactory than the fractional preparations. The great advantage of the glycerin extracts lies in the fact that they are protected against contact with air and moisture and thus retain their activity indefinitely.

The author groups for convenient reference the functions and effects produced by dysfunction of the more important glands of internal secretion, together with the means of correction of such dysfunction and the indications in which the various glandular extracts have been used. These are shown in the accompanying table, page 536.

A number of cases cited show the uniformity of results obtained by the use of standardized glycerin extracts. Comparing these with a similar group treated earlier, with varying types of products, the author found that a comparatively small dosage of glycerin extracts is effective and that the cases rate about 40 percent higher as to results achieved and period of treatment required.

TABLE OF THE MORE IMPORTANT ENDOCRINE GLANDS  
FUNCTIONS, RELATIONS AND INDICATIONS

Gland	Function	Hyperactivity	Hypoactivity	Therapeutic Action	Therapeutic Uses	Treatment of Hypoactivity
Thyroid.....	Oxidizing and detoxicating agent. Controls growth, energy production, metabolism.	Increased basal metabolism, palpitation, tachycardia, dyspnea, loss of weight, hyperactivity, nervous irritability, weakened sex desire, indigestion	Rough skin, loss of hair, mental dullness, hypotension, b & d teeth, physical defects common, cretinism, myxedema.	Regulates metabolic derangements; stimulates nutritional activity of thyroid and ovaries.	Goiter, cretinism, hypothyroidism, d & a orders of menstrual disturbances, nutritional disturbances, presenility.	X-ray or stimulation of opposing glands: Thyroid ..... 1/8 gr. Thyroid ..... 1/10 gr. Suprarenal ..... 1/40 gr. Suprarenal ..... 1/4 gr. Orchic or ovarian (male) or ovarian (fem.) 1/4 gr. Pineal ..... 1/30 gr.
Adrenals.....	Metabolism, combustion or oxidation in the body.	Increased blood pressure, rapid pulse, marked muscular strength, keen active mind, delayed peristalsis, increased red cell count.	Pigmentation, scanty hair growth, hypotension, loss of weight, low CO <sub>2</sub> content, ionkoneurosis, edema, hypersensitivity.	Regulates metabolism, promotes oxidation, increases muscular tone.	Hypoadrenalinism, heart and circulatory disturbances, asthma, tuberculosis, etc.	Rest. No glandular treatment proven effective.
Pituitary.....	Skeletal growth, carbohydrate metabolism, has strong influence on unstriated muscle.	Gigantism, coarse en- large d features, coarse and heavy hair growth, voice volume increased, sex organs frequently enlarged, impotence.	Scanty hair, pale dry skin, headache, hives, bronchitis, hypotension, easily fatigued, obesity frequent.	Stimulates, carboxy- farnthiam, pituitin, stimulates carbohydrate metabolism, promotes cell growth, increases contraction of striated muscle.	Hypopituitarism, infarction, diabetes insipidus, some headaches, to promote uterine contractions.	Extracts of opposing glands or that part of gland which is under-secreting.
Gonads.....	General metabolism and secondary sex characteristics.	Mental precocity, development of sex organs, early maturity.	Slow mentality, lack of general interest, infantilism. <i>Female:</i> Menstrual psychoses. <i>Male:</i> Effeminate traits, high-pitched voice, obesity.	Stimulates and regulates sexual development; also influences physical growth.	Sexual underdevelopment, infantilism, defective mental and physical growth, precocity.	Thymus ..... 3 gr. Ovarian ..... 2 gr. Thyroid ..... 1/10 gr. Pituitary anterior ..... 1 gr.
Thymus.....	Regulates development in childhood. Increases antitoxic powers.	Asthmatic troubles, hair and growth of opposite sex, dysmenorrhea, cardiac irregularity, whiteness of skin, bowed legs, dysplasia of neck, hyperplasia of lymphatic system.	No definite signs; may cause rashes, precocious sexual development.	Acts on metabolism, raises immunity, may promote mineralization.	Mastitis, rickets, defective bone development, low-grade and chronic infections, lymphatic troubles.	Anterior pit. 1/5 gr. Thyroid ..... 1/8 gr. Suprarenal ..... 1 gr. Orchic or ovarian ..... 1/30 gr.
Mammary.....	Regulator of lactation and to some extent of ovarian activity.	May lead to amenorrhea by inhibiting ovarian function; increases lactation.	May cause dysovarianism and menorrhagia; deficient lactation.	Stimulates lactation; regulates ovarian activity.	Deficient milk flow. X-ray; surgery.	Parathyroid ..... 1/20 gr. Orchic or ovarian ..... 1 gr. Calcium lactate 2 gr.

### VIRILISM IN WOMEN

Virilism in the female is associated with hyperfunctioning of the anterior pituitary and adrenal glands by Dr. W. Langdon Brown, London, Eng., in *Am. Med.*, Jan., 1928.

This virilism appears to vary in its manifestations according to the age at which the existing condition occurs.

During embryonic life it results in pseudohermaphroditism.

During infancy it produces hirsuties and precocious puberty; in the female it produces hypertrophy of the clitoris and immature, deformed ovaries; in the male there is testicular hypertrophy.

After puberty, hirsuties, obesity and amenorrhea are the commonest signs.

After the menopause there may be only hypertrichosis and obesity, though menorrhagia has been recorded.

The earlier the virilism is produced the greater are the structural changes.

### PARATHYROID EXTRACT IN INFANTILE TETANY

The administration of parathyroid extract is known to raise the blood serum calcium.

In *Am. J. Dis. Child.*, March, 1928, Dr. A. T. Shohl and associates report that small amounts of the extract were administered in two cases of infantile tetany. The drug had little effect on one infant. In the second case there was a control of the symptoms and an improvement, as measured by clinical and chemical results. The improvement was transitory and disappeared when treatment was stopped.

### BASEDOW'S DISEASE AND THE HEART

In *Wien. med. Wochenschr.*, May 12, 1928, Dr. N. Jagic says that both in Basedow's disease and in mild thyrotoxic cases there is a series of different heart and vascular symptoms varying in degree.

The form and size of the heart may be normal and only excessive mobility (especially of the apex) be noted roentgenologically. In severe thyrotoxicosis there may be hypertrophy and dilation of the heart, with roentgen signs of so-called mitral configuration.

As a result of muscle changes, symptoms of cardiac insufficiency may be present. Pathologic and histologic changes may be observed in the muscle, such as hyaline degeneration and degenerated areas.

In chronic Basedow's disease a prematurely developed arteriosclerosis may play a part.

Due to the changes in the heart there is, as a rule, tachycardia; rarely bradycardia; arrhythmia and extra systoles are rare. The electrocardiogram may show auricular fibrillation in severe cases.

On auscultation, a systolic murmur is frequently heard in the region of the base,

which may be regarded either as a tachycardial or a cardio-pulmonary murmur or as a sign of relative mitral insufficiency. Subjectively, there are frequently lancinating pains in the region of the heart and a feeling of oppression.

Usually there are vasomotor disturbances of different kinds, mostly peripheral; the blood pressure is, as a rule, within normal limits.

The foregoing symptoms are quite distinct from those observed in the so-called goiter heart with mechanical tracheal compression.

The treatment of the thyrotoxic symptoms in the heart and vascular systems is to give the heart rest. This is accomplished best by digitalis, quinine and sedatives.

### INSULIN

In a series of 291 cases of typical diabetes, treated by Maclean during 4 years, the net death rate was only 4 percent. Had these patients been treated on the old plan, without insulin, it may be fairly estimated that only one-third of them would still be alive.

Pregnancy has a dangerous aggravating influence on diabetes. In some such cases Labbé found insulin of excellent service.

Insulin has been used with good effect in various nondiabetic conditions. In septic conditions an increased amount of sugar is present in the blood; in such cases (excepting osteomyelitis, in which insulin is contraindicated) insulin is of benefit.

Other conditions which have been reported improved by insulin therapy are: malnutrition; vomiting; liver affections—catarrhal jaundice, cirrhosis with jaundice, malignant disease, syphilis and post-anesthetic hepatitis; also in dermatitis in which hyperglycemia seems to be a factor; in the treatment of external ulcers (applied topically); in arteritis obliterans and in angina pectoris.—*The Prescriber*, Dec., 1927.

### THE PARATHYROIDS AND FRACTURES

An editorial in the *J.A.M.A.*, May 26, 1928, calls attention to our changed conceptions regarding the functions of the parathyroid glands. Formerly their chief function was believed to be concerned with detoxication; their removal allowed an accumulation of guanidine in the system which led to tetany. Later, our ideas regarding the parathyroids were widened when Collip associated them with the regulation of blood serum calcium. This demonstration suggested the possible connection of the parathyroids with bone growth.

Ross, of McGill University, Montreal, has recently demonstrated by animal experiments that the removal of two of the parathyroids does not delay the union of fractures, but that the removal of three of them delays bony union for from four to five weeks. The excision of two parathyroids does not diminish the blood calcium level

while excision of three causes a drop of from 2 to 3 mg. of calcium per 100 cc. of serum. When the blood calcium returns to normal, bony union of fractures occurs.

Apparently a wide field of substitution therapy is opening up in connection with the parathyroids.

**THYROTOXICOSIS AND ASSOCIATED VAGOTONIC AND SYMPATHETIC COTONIC SYNDROMES**

According to Dr. Virgil E. Simpson, of Louisville, Ky., in *Am. J. Surg.*, Sept., 1927, while the manifestations attributable to either the vagotonic or sympathetic tonic group of symptoms in thyrotoxicosis may be kept in mind during the clinical study of a case and set down in a record of physical findings, yet they will be disconnected. Dr. Simpson has found it convenient to keep them grouped as follows in order to make an intelligent summary at the close of the study:

**Vagotonia**

1.—Eye:

Narrow palpebral fissure  
Blepharospasm  
Infrequent winking  
Enophthalmos  
Epiphora  
Accommodation spasm  
Myosis

2.—Skin:

Hyperhydrosis  
Acrocytosis  
Dermatographia  
Acne  
Hyperresponsiveness to pilocarpine

3.—Respiratory System:

Irregular respiration  
Bronchial asthma  
Laryngospasm  
Husky voice

4.—Circulatory System:

Arrhythmia  
Bradycardia  
Eosinophilia  
Pseudoanginal attacks  
Erythromelalgia

5.—Digestive System:

Diminished gag reflex  
Increased salivary flow  
Esophagismus  
Cardiospasm  
Hyperchlorhydria  
Pylorospasm  
Gastric hypertonia  
Reflex vomiting  
Mucous colitis  
Tender colon  
Spasm of sigmoid  
Constipation  
Viscerotonia  
Visceral crises  
Aerophagia

6.—Nervous System:

Insomnia  
Mental irritability  
Sexual hyperexcitability  
Nervous chills

Easy fatigue  
Lack of confidence

7.—Metabolism:

Increased sugar tolerance  
Increased fat tolerance  
Status thymolymphaticus

**Sympathicotonia**

1.—Eye:

Mydriasis  
Myosis on forced inspiration  
Myosis on forced expiration  
Wide palpebral fissure  
Diminished lacrimal secretion  
Winking lacrimal secretion  
Prominence of eyeball  
Faulty convergence  
Loewe test negative

2.—Skin:

Urticaria  
Angioneurotic edema  
Facial pallor on emotion  
Hypohydrosis  
Cutis anserina  
Pigmentary anomalies  
Canities, unilateral or bilateral  
Psychic flushing  
Salivation not increased by pilocarpine

3.—Respiratory System:

Dyspnea  
Tachypnea

4.—Circulatory System:

Precordial distress  
Palpitation  
Exaggerated amplitude of cardiac contractions  
Apical impurity after fatiguing exercise  
Pulsation of superficial vessels  
Capillary pulsation  
Tachycardia, orthostatic  
Vasomotor lability  
Respiratory arrhythmia  
Aschner's phenomenon  
Goetsch's test

5.—Digestive System:

Intestinal colic  
Nervous diarrhea  
Hypocholesterolemia  
Gastric atony  
Lessened secretions of gastrointestinal tract  
Diminished salivary secretion  
Lessened peristalsis of intestine  
Hypertonicity of intestinal sphincter  
Painless dysphagia  
Gag reflex, increased

6.—Nervous System:

Neuroses  
Psychoses  
Emotional polyuria  
Pollakiuria  
Exaggerated emotivity

7.—Metabolism:

Low sugar tolerance  
Alimentary glycosuria

The presence or absence of these symptoms is designated by + or - signs, these being doubled or trebled according to the intensity of the symptoms.

The difficulty of determining whether vagotonic or sympathetic symptoms predominate is overcome by this method and, since both sets of symptoms occur in thyrotoxicosis, the matter is simplified.

Certain of the endocrine hormones act through the vagal division alone, while others act through the sympathetic or through both. The adrenals are active, powerful sympathetic agents, while the pancreas exercises an equally selective effect on the vagal division. When there is a disturbance of the balance between the two systems endocrine secretion therapy can be determined accordingly.

#### THYROID THERAPY OF CHILDREN

Drs. Anne Topper and P. Cohen, New York, in *Am. J. Dis. Child.*, Feb., 1928, found that, in 4 children with subnormal basal metabolism and clinical manifestations of hypothyroidism, thyroid, in small or moderate doses, promptly brought the basal metabolism rate to a normal level, where it stayed even after thyroid therapy was discontinued.

In 9 children with a normal basal metabolic rate, as much as 15 grains of thyroid extract daily did not increase the basal metabolism, although 4 of these children showed a remarkable increase in growth during this period.

The action of thyroid on normal children seems to be different from its action on normal adults.

#### THE FEMALE HORMONE

The female sex hormone as a therapeutic agent must be considered as still in an entirely experimental stage. The outlook for it, however, would be extremely promising were it not for the great difficulty of obtaining concentrated solutions, as well as the great expense involved in purchasing the raw material, fresh ovaries now marketing at the price of over one dollar a pound.

—DR. ROBT. T. FRANK, in *Am. J. Obst. & Gynec.*, Jan., 1928.

#### THE MALE FACTOR IN STERILITY AND ABORTION

Until comparatively recently, all responsibility for an infertile human union has been laid upon the female, and many women have been extensively tinkered with, in an effort to make them bear children, under circumstances where we would now readily recognize that the man was entirely to blame.

The problem of sterility still offers a wide field for study, and Dr. Gerard L. Moench, of New York, has made a contribution toward its solution in *Med. Herald and Physiotherapist* for March, 1928.

After discussing the well known causes of sterility in some detail, Dr. Moench describes his researches regarding abnormali-

ties in the structure of the spermatozoa, using charts and drawings to illustrate his points, and suggests that, even though a man's semen may contain considerable numbers of motile sperm cells, he may still be the conjugal partner responsible for sterility, if most of these cells are of abnormal type. He goes even further and suggests that abnormal sperms may possibly be the cause of repeated abortions, this being nature's method for getting rid of unnatural products of conception.

This is a long treatise and shows much study and labor in its preparation, and while it cannot be more extensively abstracted here, we suggest that those who are sincerely interested in this subject should write to the author, at 30 E. 58th St., for a reprint of what appears to be a rather important contribution toward the understanding of sterility.

#### ROENTGEN THERAPY IN HYPER-THYROIDISM

In *M. J. & Record*, Feb. 1, 1928, Dr. Wm. H. Meyer, of New York, reports his experiences in 328 cases of thyrotoxicosis subjected to x-ray treatment during the past ten years.

The principal findings which experience have justified are as follows:

1.—In cases of adolescent goiter with evidence of hyperfunction, the latter can frequently be relieved with three to five x-ray treatments.

2.—In tumors of the thyroid, if the basal metabolic rate be definitely increased, three or four treatments will usually reduce the signs of hyperfunction and thereby render the case safer for operation. More rarely will continued treatment result in sufficient reduction of the tumor to render operation unnecessary. Also in substernal thyroids or where pressure symptoms supervene these may be relieved by a more protracted course of treatments. On the whole, tumors of the thyroid gland do not appear to be generally suitable for roentgen therapy except as above mentioned.

3.—The influence of iodine upon thyroid hyperfunction is only temporary, in many cases.

4.—With frank cases of Graves' disease, experience tends to substantiate the claim that roentgen therapy has a definite place in the treatment. A total of 84 percent of the cases of Graves' disease show definite improvement. Of this number, 66 percent of the patients are either symptom-free or within the normal limits of the metabolic test.

5.—In Graves' disease the x-rays are not immediate in action; reaction is, as a rule, delayed, with a quite protracted period of treatment and waiting. Therefore, seriously acute, febrile and markedly psychotic cases do not appear to be suited to immediate x-ray therapy but should be put at complete rest under symptomatic treatment.

In the face of the otherwise generally satisfactory results obtained by roentgen

therapy in Graves' disease, the large percentage of failures occurring after the administration of iodine argues strongly against the use of this drug.

#### LIVER EXTRACT IN ECLAMPSIA

In the *Weekly Roster and Med. Digest*. (Philadelphia) February 4, 1928, Dr. Harold A. Miller, of Pittsburgh, stated that 780 pre-eclamptic women (judged by objective and subjective symptoms) and 25 actually convulsing women were treated by "Heparmone" (liver extract). Of these, 39 should ordinarily have been expected to develop toxic symptoms. All patients went into labor spontaneously, with no maternal mortality. No mortality occurred among the pre-eclamptic cases; no convulsions occurred in any adequately treated case.

Dr. Miller thinks an eclamptic woman should be given 20 cc. of Heparmone as soon as seen; blood pressure should be taken every 15 minutes and enough Heparmone given to bring it to normal. For five to six days after convulsions, 15 cc. of Heparmone are given intramuscularly three times a day.

Mild cases receive one injection of 10 cc. per week; moderate cases receive 10 cc. every second day. The criterion is the blood pressure.

#### SCIENTIFIC ENDOCRINE RESEARCH

The real reason why such noticeable advances have been made in endocrinology during the last decade is solely due to the fact that the pharmacologist, physiologist and chemist have finally supplanted the empiric investigator. Each advance has been based upon the discovery or elaboration of some specific and pathognomonic test for a given endocrine product. Without such specific test it is almost impossible to attempt either to find, purify, or isolate a hormone.—DR. ROBT. T. FRANK, in *Am. J. Obst. & Gynec.*, Jan., 1928.

#### OVARIAN CYCLE AND INSULIN

The effects of insulin on the activity of the female glandular secretions is discussed by Dr. E. Vogt, in *Med. Klinik.*, Beihefte 7, 1927.

Hemorrhages resulting from ovarian dysfunction are relieved by insulin; but hemorrhages arising from endometritis and tumors are not affected by it. In general, the conditions in non-diabetics for which insulin therapy is valuable are: metrorrhagia, menorrhagia, metabolic disturbances in premature births, alimentary intoxications, hyperemesis gravidarum and postoperative acidosis.

The strength of the insulin effect is dependent on the ovarian cycle—on the con-

tent of the blood in ovarian hormone or in female sex hormone—and is very uniform during the second half of pregnancy, during which the ovarian hormone in the blood is gradually increased.

Insulin, as the pancreas hormone, has exactly the same effect as an ovarian preparation, in that it increases ovarian activity and equilibrates its hypofunction.

It is best to begin with a moderate dosage of 20 to 30 insulin units, distributed in 2 subcutaneous injections, before the midday and evening meal. As hemorrhages are arrested after two or three days, the danger of insulin injury is much decreased.

A course of treatment should never be begun nor should dosage be raised during the second half of the intermenstruum. During menstruation injections of insulin should be discontinued.

Vogt has also found that it is possible to sterilize female rabbits by long-continued doses of insulin.

#### THE OVARIAN HORMONE

A. Biedl, in *Arch. f. Gynaek.*, v. 132, p. 132, p. 167, 1927, states that he has succeeded in preparing from follicular fluid, as well as from whole ovary, free from follicle and corpus luteum, a water-soluble substance which exhibits all the properties of the estrus hormone. The preparation was found therapeutically effective in cases of juvenile amenorrhea and climacteric complaints.

Further investigations, with respect to the relation of the pituitary to the ovarian secretion, justified the conclusion that a pituitary inhibitory hormone exists which arrests the estrus cycle and ovulation.

#### X-RAYS AND THE ENDOCRINES

In *Radiology*, for October, 1927, Dr. H. L. Wintz, of Erlangen, states that four distinct effects upon the endocrine glands can be produced by x-rays, according to the way they are used.

- 1.—Complete destruction of the gland.
- 2.—Total, but temporary, impairment of its activity.
- 3.—Destruction of the more sensitive cells, while sparing those that are less sensitive.
- 4.—Stimulation of the activity of the gland.

When temporary sterilization is obtained by raying the ovaries, the other endocrine glands are not disturbed; but when the ovaries are destroyed by x-rays, the symptoms of surgical menopause come on.

In hyperthyroidism of ovarian origin, temporary sterilization should be performed. In hypothyroidism of ovarian origin, both thyroid and ovarian extracts should be administered, without raying. Similar relationships exist between the ovary and the thymus and pituitary glands.

# New Books

## COBB: ORGANOTHERAPY

**AIDS TO ORGANOTHERAPY.** By Ivo Geikie Cobb, M.D., M.R.C.S., Neurologist, Ministry of Pensions; Late Assistant to Out-Patient Physician, The Middlesex Hospital; etc. New York: William Wood & Company. 1927. Price \$1.50.

This small volume is intended by its author as an introduction to the study and practice of organotherapy, and as gland extracts are now largely used to replace the crude substance, much the greater part is concerned with the endocrine extracts.

Dr. Cobb has wisely devoted very considerable space to the thyroid-parathyroid apparatus, as more is known with certainty regarding these glands, their functions and the therapeutic action of their extracts than of the other endocrine organs. The inclusion of chronic rheumatism, certain skin diseases and nocturnal enuresis under thyroid diseases will be unfamiliar to many.

The book is only an outline. It is written in a simple style and gives a good introduction to a more elaborate work on the functions and therapy of the endocrine glands and other organs.

Physicians who have had little or no experience with organotherapy will find this a sane and practical work to prepare them for beginning to use glandular extracts, which should now be a part of every medical man's armamentarium.

## McCARRISON: SIMPLE GOITERS

**THE SIMPLE GOITERS.** By Robert McCarrison, C.I.E., M.D., D.Sc., LL.D., F.R.C.P., Associate Fellow of the College of Physicians, etc. New York: William Wood & Company. 1928. Price \$4.00.

Dr. McCarrison's book is an amplification of a report made to the International Conference on Goiter, held at Berne, Switzerland, in 1927.

Though short, the work is important, not only on account of the reputation of the author in the fields of endocrinology and nutritional physiology, but because his conception of the etiology of goiter differs essentially from the more or less accepted view that endemic goiter is the result of iodine deficiency in food and drinking water.

Dr. McCarrison's long researches in India and his experimental production of goiter have satisfied him that the chronic, hypertrophic type of endemic goiter is due to a positive toxic agent derived from the gastro-intestinal tract. The immediate causative factor is drinking water polluted with such a toxic agent.

Dr. McCarrison is also of the opinion that "the indiscriminate use of iodine as

a preventative of 'goiter' is a procedure both unscientific and dangerous."

A very large number of illustrations and charts accompany the text, which is a notable addition to goiter literature and should be in the possession of everyone interested in this widely diffused disease.

## DOPPLER: CHEMICAL STIMULATION OF SEX HORMONE

**ÜBER TECKNIK UND EFFEKTEN DER SYMPATHIKODIAPHTHERESE AN DEN KEIMDRUSENARTERIEN.** Vortag, gehalten am 30. März 1928 im Verein Deutscher Ärzte in Prag, in erweiterter Form. Für Ärzte und Biologen Von Dr. Karl Doppler, Assistant der Abteilung Berlin und Wein: Urban & Schwarzenberg. 1928. Price RM. 2.

The author describes a method of chemical activation of sex gland hormone production, if deficient, by the action of a phenol solution (Iophenol) on the sympathetic innervation. The method is offered as a substitute for the Voronoff and Steinach operative methods.

## BERMAN: GLANDS OF PERSONALITY

**THE GLANDS REGULATING PERSONALITY.** A Study of the Glands of Internal Secretion in Relation to the Types of Human Nature. By Louis Berman, M.D., Associate in Biological Chemistry, Columbia University. Second Edition, Revised. New York: The Macmillan Company. 1928. Price \$3.50.

The public is becoming interested in the endocrine glands, as shown by the considerable demand for several half-digested and sensational books on the subject which have appeared.

Dr. Berman has realized the need for an accurate and reliable discussion of the subject, in language understandable by a layman, and has attempted to meet that need.

The average lay reader wants even his scientific and instructive literature highly-flavored and dramatic—otherwise he is apt not to go very far with it. In recognizing and catering to the popular taste, the author has set forth references and speculations which will at once be recognized, by scientific students, as being somewhat far-fetched. But the basis upon which these theories are erected is sound and valid, and the future may well prove them to be correct. In any case, they are interesting.

It is to be regretted that, in giving us a popular book on this important subject, Dr. Berman has not seen fit to condense his material. Few intelligent and active people in these busy days, will take the time to read 330 closely-printed pages of text, unrelieved by illustrations, on a technical subject, even though it is pleasingly presented.

If the same ground upon which he spreads about 130,000 words had been covered in 60,000 to 75,000, the type might have been larger and the pages more open and easy to read, without increasing the size of the book. Moreover, the information could, one feels, have been more clearly and pleasingly presented in fewer words. Pictures would help, also.

Those who will take the time and put forth the effort to read this volume will find much of interest and real value in it, for the author knows whereof he speaks, and when he makes statements of known facts they seem all to be verifiable.

It is a book which physicians can safely recommend to inquiring patients who have the time to read a long and pleasant book.

#### CROFTON: ENDOCRINOLOGY

**AN OUTLINE OF ENDOCRINOLOGY.** By W. M. Crofton, B. A., M.D., Lecturer of Special Pathology, University College, Dublin; Pathologist, Dr. Stevens' Hospital, Dublin. Edinburgh: E. & S. Livingstone. New York: William Wood & Co. 1924. Price \$2.25.

To the medical student and to the practitioner who has not made a study of the anatomy and physiology of the glands with an internal secretion, a short handbook, such as Dr. Crofton has written, will be very acceptable. The book has been specially designed for this purpose. While only an outline, it contains all the essential facts, gleaned from the most reliable sources, and there are many illustrations of both gross and histologic appearances, which are very helpful in elucidating the text descriptions.

In addition to anatomy and physiology, the pathologic conditions arising from glandular dysfunctioning are sketched and the therapeutic aspects also receive brief attention.

As a book for quick reference and an introduction to ooothotherapy this small volume can be recommended to practitioners.

#### PETTY: DIABETES

**DIABETES. Its Treatment by Insulin and Diet. A Handbook for the Patient.** By Orlando H. Petty, A.M., M.D., F.A.C.P., Professor of Diseases of Metabolism, Graduate School of Medicine, University of Pennsylvania; etc. With Illustrations and Tables. Fourth Revised and Enlarged Edition. Philadelphia: F. A. Davis Company. 1928. Price \$2.00.

The main object of Dr. Petty's book, which has now reached the fourth edition, is the education of the diabetic in all matters pertaining to his health.

The dietary and insulin treatment and control are given special prominence. The book is not intended as a substitute for the physician's advice but rather as a help, so that the patient may become an intelligent cooperator in his own treatment.

There are ten chapters and the book is written in an easy style, the plain language used being easily understood by a patient of average intelligence.

The important point seems to us to lie in the fact that hope of a definite cure is held out to the patient.

#### HOBGEN: INTERNAL SECRETIONS

**THE COMPARATIVE PHYSIOLOGY OF INTERNAL SECRETION.** By Lancelot T. Hogben, M.A. (Cantab.), D.Sc. (Lond.), Professor of Zoology in the University of Capetown. New York: The Macmillan Company. Cambridge, England: The University Press. 1927. Price \$4.00.

Within the past twenty-five years, probably no part of medicine has received more attention than endocrinology, around which practically a new branch of medical science has developed.

Professor Hogben's book deals with the comparative physiology of the internal secretions in coordinating the activities of the organism and is written from the viewpoint of the zoologist.

The book may properly be regarded as a collected and connected review of the literature dealing with the physiologic functions of the endocrines, especially in animals. There is but little of practical value to the clinician, except insofar as he may be interested in following the scientific developments of research in the subject discussed.

#### HARROWER: ANABOLIN AND HYPERTENSION

**THE HEPATIC PRINCIPLE, ANABOLIN, DETOXIFICATION BY THE LIVER AND THE CONTROL OF FUNCTIONAL HYPERTENSION.** By Henry R. Harrower, M.D. With a Foreword by Ivo Geikie Cobb, M.D. And an Historical Introduction by Victor Robinson, M.D. London: Baillière, Tindall and Cox, 7 and 8, Henrietta Street, Covent Garden, W.C. 2. 1927. Price \$3.00.

From time immemorial, speculation upon the liver and its functions has loomed large in the development of medical science.

In the monograph under review, Dr. Harrower sets out to establish the following propositions: (1) that the liver is a gland of internal secretion with its endocrine influence involving its detoxicating service; (2) that the product known as Anabolin is an original substance, practically previously unknown, separated from the liver cells, first prepared under the author's direction and which has a clear therapeutic advantage in the treatment of certain toxemias accompanied by hypertension; (3) that the effects produced by Anabolin are not due to peptone or protein shock; (4) that the effects of Anabolin upon functional hypertension are so marked as to support the author's conviction that it is the internal secretion of the liver; (5) that its therapeutic use has not been followed by harmful results.

These propositions Dr. Harrower supports by arguments resting upon medical literature which is largely quoted.

The various chapters throw a flood of light upon the functions of the liver and the mechanism by which these functions are manifested.

The great importance of the liver and the comparative indifference of the majority of practitioners toward recent developments regarding it should insure a welcome for Dr. Harrower's synopsis of our present knowledge of liver physiology.

#### GLANDULAR THERAPY

**A COMPENDIUM OF GLANDULAR THERAPY.** *New York: Colwell Pharmacal Corporation, 25 Church St.* 1927. Price \$1.50.

This little compendium of glandular therapy will give a concise general review of the subject which will be found useful to physicians who are not well acquainted with this branch of medicine. Physicians who are acquainted with glandular therapy will find the literature up to the present time summarized in a consecutive form.

#### MILLER: THYROID SURGERY

**SAFEGUARDED THYROIDECTOMY AND THYROID SURGERY. A Manual Designed as a Practical Guide for the General Surgeon.** *By Charles Conrad Miller, M.D., With Fifty-two Illustrations.* Philadelphia: F. A. Davis Company. 1928. Price \$3.75.

Although there is no dearth of periodical literature dealing with every aspect of goiter surgery, yet Dr. Miller has felt that there are many practical points omitted from the current textbooks and these he has endeavored to supply in the book under review.

The first part of the book deals with the clinical aspects of thyroid dysfunction, especially those of hyperthyroidism, and its diagnosis.

While the medical treatment of goiters is satisfactory in a large percentage of cases, yet economic factors prevent many patients from availing themselves of it and surgery offers a quick and safe means of remission.

Dr. Miller says that the surgery of goiter is very easy and safe when the operator is adequately informed. For this reason he enters fully into all the technical details connected with thyroid surgery and the precautions which are necessary, especially in connection with the parathyroids and the vessels in the vicinity of the gland. The chapters on thyroid surgery from the standpoint of the general surgeon, on the technic of the safeguarded operation of thyroidectomy, and on the modifications of thyroidectomy are especially illuminating and well illustrated.

Besides goiter, the volume also deals with the surgical treatment of other conditions of the thyroid, including malignant tumors.

Dr. Miller feels that more general surgeons would do goiter surgery if its safety

could be impressed upon them; also that adequate surgery produces a prompt remission, in patients who have not benefited by medical treatment.

This is a practical book, every chapter in which contains useful, applicable information, not alone for the surgeon but for the general practitioner. The general surgeon will find the technical details of thyroid operations very clearly and fully described; he will know what to do and what not to do in the types of cases which are ordinarily met with; and the factors which make for safe operating will especially be of value to him.

#### LAMBERT: PSYCHIC PHENOMENA

**A GENERAL SURVEY OF PSYCHICAL PHENOMENA.** *By Helen C. Lambert. Foreword by Stanley De Brath.* New York: The Knickerbocker Press. 1928. Price \$2.50.

A generation ago, the serious mention of psychic phenomena was enough to set the neighbors to wondering if a case were not brewing for the alienists. Today the mass of solid, scientific evidence has become so great that no open-minded thinker can afford to dismiss it with a shrug and a wink.

There is no dearth of works on the subject, but most of them are so technical as to be beyond the grasp of the ordinary reader; or they contain detailed and lengthy records of laborious experiments under meticulously controlled conditions, which are tiresome to all except enthusiastic investigators.

A need has been felt for a book setting forth, simply and straightforwardly, the elementary facts of psychic science as it now stands, in such a manner as to be comprehensible to people who wish to keep abreast of modern thought, but do not desire to enter upon a deep study of the question. Such a book Mrs. Lambert has undertaken to give us. It is a study of the mental realities, or *noumena*, which underlie the physical realities, or *phenomena*.

Richelet is quoted, to the effect that a thousand negative facts prove nothing, in the face of one which is positive.

Anyone who is seeking information on psychic matters merely to satisfy an idle or morbid curiosity, had best let the subject alone; and those who decide to investigate on their own account must select their companions in such efforts with the keenest discrimination. Moreover, amateur experimentation must not be dignified as "psychic research," any more than looking at a drop of blood under the microscope would be considered biologic research.

The first chapter deals with physical phenomena, which are declared to be relatively unimportant, though they are persistently called for by the materialistic scientist; and the second with mental phenomena, which are far more vital and no less scientific. In studying these latter facts, one must guard against stretching the idea of telepathy to ridiculous extremes, and accept

the simplest explanation consistent with the facts and with reason.

The chapter on Evidence is excellent. Many people feel that the lines of "scientific proof" have been drawn arbitrarily and that, so far as objective results are concerned, we have as much reason for rejecting many of the postulates of astronomy and physics as we have for sneering at those of psychic science; also that deductions based upon a long series of careful observations should be given more weight than negations based solely on prejudice.

The fourth chapter is devoted to the evidences for the survival of individual consciousness beyond physical death, and is decidedly convincing.

The second part, comprising about half of the book, is a record of the personal psychic experiences of the author, given in full detail and backed up by the names of witnesses and by copies of letters. These are set forth in an unemotional but very interesting manner.

No up-to-date physician can, today, afford to be wholly ignorant of the work being done in psychic research, and this modest but well-made volume will give him a sound basis of valid information.

#### COBB: GLANDS OF DESTINY

**THE GLANDS OF DESTINY. (A Study of the Personality).** By Ivo Geikie Cobb, M.D. New York: The Macmillan Company. 1928. Price \$3.00.

In the ancient days the humoral pathologists connected the characteristic traits of human personality with the prevalence of certain "humors" in the body. These were spoken of as melancholic, choleric, bilious, etc., such types being assumed to result from an excess of the humors called melancholia (black bile), cholera (bile), etc., in the body fluids.

Today we have come back to the same thing, only we call the "humors" by more scientific terms, designating them as secretions of the endocrine glands.

The study of personality and of all the factors which constitute it, as set forth in Dr. Cobb's book, is most fascinating.

The author of this very readable volume shows us how cranial and other morphology affects the development of certain glands; how this development affects the physical and psychic characters; also how food, habits and customs may influence our glands and our personality complex in the same way. In fact, in a sense, we become what we eat, because certain substances, acting through the blood, can be made to affect,

directly, the glands governing personality in individuals and races.

One cannot help thinking, on glancing through this book, that we are to a great extent what we make ourselves; but on the other hand we have still a long road to travel in arriving at correct methods of applying the knowledge gained.

Dr. Cobb's book contains fourteen chapters, together with a glossary and bibliography. It may be described as a popular presentation of facts and surmises regarding the influences which the products of the glands of internal secretion exert through the blood (and perhaps other body fluids), in shaping the morphologic and psychologic human traits. Any intelligent layman can easily follow it, and all physicians who are not already deep students of endocrinology will find it interesting and helpful in their work.

#### FOSTER: EXAMINATION OF PATIENTS

**THE EXAMINATION OF PATIENTS.** By Nellis B. Foster, M.D., Associate Physician to the New York Hospital; Associate Professor of Medicine at Cornell University College of Medicine. Second Edition, Revised. Philadelphia and London: W. B. Saunders Company. 1928. Price \$4.50.

The value of clinical medicine rests on accurate diagnosis. It is not too much to say that most of the failures in medicine are not the result of inefficient therapeutic methods, but of insufficient and inaccurate examination of the patient and the failure to understand the nature of his disease. Hence, such books as Dr. Foster's are of very distinct value to the practitioner, because they show how a systematic examination should be made, what to look for, what to expect from the patient's history and how objective symptoms should be evaluated and counterchecked.

Dr. Foster's book is based upon his experience as a hospital clinician. It rounds out the classical descriptions given in textbooks with the innumerable details which can be acquired only by daily clinical practice and by the study of the idiosyncrasies of different patients with the same general disease conditions. Such clinical experience and acumen are now being recognized as a necessary equipment, laboratory methods being regarded as secondary.

In the present (second) edition, methods of differential diagnosis are included. Special attention is given to the clinical findings in cases of diseases which are most prevalent in the United States, particularly those of the respiratory and digestive systems.

Dr. Foster's book should be of value to every practitioner.

# Medical News



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## DR. HARDING HEARTY AT 84

Dr. George T. Harding, father of the late President Harding, is a veteran of the Civil War and at the age of 84 years is still keenly interested in what is going on in the world.

He is shown seated before the flag he helped to defend.

## NOGUCHI A MARTYR TO SCIENCE

Prof. Hideyo Noguchi, bacteriologist of the Rockefeller Institute for Medical Research, died from yellow fever, which he was investigating, at Accra, Gold Coast, Africa, May 21, 1928. He used his own last illness, which lasted for several months, to complete some very important data on the disease which he was studying. A monkey inoculated with his blood was the first laboratory animal ever to develop yellow fever.

Three scientists have now given their lives in the prosecution of these important researches. Dr. Adrian J. Stokes died of

yellow fever in September, 1927; then Noguchi; and on May 30, 1928, Dr. William A. Young, an American worker with the Rockefeller Institute, surrendered his life in the cause of science.

The demonstration by these martyrs that monkeys are susceptible to this disease will have far-reaching effects, for it can now be studied in the laboratory.

## AN OPENING IN INDIANA

There is said to be a good opening for a qualified physician 30 to 40 years of age in a live town of about 4,000 in northern Indiana. An office, with equipment, can be rented at the start. Further particulars may be obtained from V. S. Huffman, D.V.M., Route 5, Columbia City, Ind.

## POSITION FOR A RECENT GRADUATE

Occasionally a young man who has recently graduated in medicine prefers to take up one of the side lines of the profession, rather than engage in actual practice. Details of an opportunity for this kind of work may be had by addressing Dr. G. D. Searle, 4753 Ravenswood Ave., Chicago.

## ANGLO-AMERICAN PHYSICIANS IN EUROPE

The American traveling through Europe not infrequently comes in contact with evidences of European mentality that strike him as rather incomprehensible. It has recently been brought to our attention that Americans traveling on the Continent are unable to secure from the management of the hotel where they are staying the name and address of an American or English physician. All knowledge of such is usually denied, but they can always supply the name of a doctor of their own nationality who "speaks English perfectly." When this doctor appears, it is only rarely that he can speak sufficient English to make himself understood.

The Continental Anglo-American Medical Society publishes a list of the American and English doctors practicing in Europe, and this list ought to be in the hands of

every American going abroad. A copy can be secured by any one, free of charge, by addressing a request to the Secretary, Dr. Sherwood-Dunn, 54, Boulevard Victor Hugo, Nice, France.



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#### DR. WALSH DESIGNS HOSPITAL EMBLEM

The American Hospital Association has voted to adopt an emblem which signifies the service rendered by such an institution. The design was worked out by Dr. William H. Walsh of Chicago, executive secretary. The colors are white, gray, red, blue and gold. The insignia will be embroidered on attire worn by nurses while on duty and will also be used on stationery in use among hospitals and in other ways, as a distinctive emblem to call to mind the Association and the things for which it stands.

#### DEBATES WITH CULTISTS

Little good to anyone concerned can come from public debates between physicians and faith healers, antivivisectionists, antivaccinationists and representatives of like cults. An unbiased audience and a fair hearing are unlikely.

We will do better to confine our educational efforts to individual instruction and the publication of the truth in popular periodicals.

#### SCHOOL OF TUBERCULOSIS

The Chicago Municipal Tuberculosis Sanitarium is offering a comprehensive program of instruction in all features of tuberculosis, including a course for undergraduates, resident clerkships, graduate instruction, post-graduate course for practicing physicians, special courses and research scholarships. They have an excellent faculty, modern facilities and a wealth of clinical material.

The School of Tuberculosis of the Municipal Tuberculosis Sanitarium will conduct, during the month of August, a course in postgraduate study. The course, which will last the entire month, will cover in detail the clinical, laboratory and public health aspects of tuberculosis. It is free of charge except for a nominal diploma fee and is open to all Chicago and out-of-town physicians who are interested in the subject of tuberculosis. Address inquiries to Dr. Benjamin Goldberg, Director, School of Tuberculosis, 2049 Washington Boulevard, Chicago, Illinois.

#### CENTENARY OF WM. S. MERRELL CO.

On June 10, 1828, William Stanley Merrell opened an apothecary shop, which later developed into the Wm. S. Merrell Company, manufacturing pharmacists.

Merrell introduced a number of resins and resinoids as therapeutic agents, including podophyllin, hydrastin, macrotin, iridin, and a number of others. The American College of Medicine, at Philadelphia, gave him the degree of Doctor of Medicine *honoris causa*.

The firm founded by Dr. Merrell has given the medical profession sincere service for a century and is steadily growing.

#### DERMATOLOGY NUMBER

The May, 1928, issue of *American Medicine* is devoted entirely to dermatology and contains 27 original articles.

Our worthy contemporary has done a good piece of work and has given the profession what almost amounts to a modern textbook on skin diseases.

# Send for This Literature

To assist doctors in obtaining current literature published by manufacturers of equipment, pharmaceuticals, physicians' supplies, foods, etc., CLINICAL MEDICINE AND SURGERY, North Chicago, Ill., will gladly forward requests for such catalogues, booklets, reprints, etc., as are listed from month to month in this department. Some of the material now available in printed form is shown below, each piece being given a key number. For convenience in ordering, our

readers may use these numbers and simply send requests to this magazine. Our aim is to recommend only current literature which meets the standards of this paper as to reliability and adaptability for physicians' use.

Both the literature listed below and the service are free. In addition to this, we will gladly furnish such other information as you may desire regarding additional equipment or medical supplies. Make use of this department.

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- G- 1 Helping the Cell to Help Itself. 32-page booklet by The Alkalol Co.
- G- 2 Your Prestige and Profit. 8-page booklet. The Carroll Dunham Smith Pharmacal Co.
- G- 3 Storm Binder and Abdominal Supporter. 4-page folder by Dr. Katherine L. Storm.
- G- 4 Pluto Water. Its Medicinal Values. 16-page booklet. French Lick Springs Hotel Co.
- G- 5 Ethical Medicinal Specialties. 8-page booklet. A. H. Robins Co.
- G- 6 The Journal of Organotherapy. 95-page booklet published monthly. G. W. Carnrick Company.
- G- 7 The Cure of Cystitis, Pyelitis and other Inflammatory Conditions of the Urinary Tract. Chicago Pharmacal Co.
- G- 9 Hang This Up—It Tells How to Make Percentage Solutions. Sharp and Dohme.
- G- 14 The New Ultra-Violet Therapy. McIntosh Electrical Corporation.
- G- 17 An Index of Treatment. Burnham Soluble Iodine Co.
- G- 20 A Survey of Focal Infection. Fellows Medical Co.
- G- 37 pH 7.4, Alka-Zane. Wm. R. Warner & Co., Ltd.
- G- 38 Hycol. The Certified Disinfectant. Merck & Co.
- G- 39 A Convincing Solution of an Old Problem, Isacen. The Hoffmann-La Roche Chemical Works.
- G- 40 Truth Spreads by Testimony, Isacen. The Hoffmann-La Roche Chemical Works.
- G- 41 The Specific Treatment of Pneumonia with Numoquin Base. Merck & Company.
- G- 42 Detoxification in the Treatment of Infection. The Wm. S. Merrell Company.
- G- 43 "Humanize" Cow's Milk. The Wm. S. Merrell Company.
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- G- 47 Campho-Phenique in Major and Minor Surgery. Campho-Phenique Company.
- G- 49 The Calcreose Detail Man. Maltbie Chemical Co.
- G- 50 Outwitting Constipation. Standard Oil Co.
- G- 51 The Ideal Anti-Gonorrhoeic. Riedel & Co., Inc.
- G- 52 Cre-So-Mul. First Texas Chemical Mfg. Co.

G- 56 Regaining Health. How Science Can Guide You! The Fleischmann Company.

G- 58 The Pharmacology of Cod Liver Oil. Smith, Kline & French Co.

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G- 70 Yeast Therapy. The Fleischmann Company.

G- 78 Nourishment for Adults and Children in Health or Illness. Mellin's Food Co.

G- 82 Service-Suggestions, May-June, 1928. Victor X-Ray Corp.

G- 84 Latent Constipation—A Diagnostic Problem, Agarol. Wm. R. Warner & Co.

G- 85 Ultraviolet for Health. Hanovia Chem. & Mfg. Co.

G- 87 Journal of Intravenous Therapy. Loeser Laboratory.

G- 93 Britesun Therapeutic Booklet. Britesun, Inc.

G- 94 A Compendium of Glandular Therapy. Colwell Pharmacal Corporation.

G- 95 Everything for the Sick — Lindsay Laboratories.

G-103 The Electron. McIntosh Electrical Corporation.

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G-127 The Surgical Treatment of Goiter. The C. V. Mosby Co.

G-128 A New Book Written in Simple Language, Getting Well and Staying Well (Tuberculosis). The C. V. Mosby Company.

G-129 Ultra Violet Therapy. Britesun, Inc.

G-134 Loeser's Concentrated Salt Solution. Loeser Laboratory.

G-135 Enemata — Petrolagar. Deshell Laboratories, Inc.

G-136 Obesity in Females. The Tilden Company.

G-137 The Treatment of Malarial Anemia. Loeser Laboratory.

G-139 How to Save Children from Goiter. Morton Salt Company.

G-140 Treatise on Blood Dyscrasia and Allied Lesions. Strong, Cobb & Company.

G-144 In Habitual Constipation. Pitman-Moore Company.

G-145 Victor Thermospectral Lamps. Victor X-Ray Corporation.

G-146 Why Thyroid and Ovary Together. The Harrower Laboratory, Inc.

G-147 Ephedra. Physiologic and Therapeutic Report. The National Drug Company.

G-148 The Quartz Lamp, May 15. Hanovia Chemical & Mfg. Co.

G-149 Zinc Ionization for Chronic Otorrhea. Victor X-Ray Corporation.

G-150 The Sollux Radiant Heat Lamps. Hanovia Chemical & Mfg. Co.

G-151 Merrell's Ampoules for Subcutaneous, Intramuscular, Intravenous Use. The Wm. S. Merrell Company.

G-152 The Invisible Mask. Strong, Cobb & Company.

G-153 Caprokol. Sharp & Dohme.

G-154 Medical Pocket Quarterly, June. Reed & Carnick.